STUDIES OF THE RESPIRATORY FUNCTION

IN MENTAL DISORDER

by

ARTHUR SPENCER PATERSON,

M.A.(Oxon), M.B., Ch.B., F.R.C.P.E.
Dipl. Psych.

Introduction.

The pathological processes in the more serious forms of mental disorder, especially those now grouped under the title of schizophrenia, have long proved a peculiarly difficult subject for scientific study. While men such as Kraepelin did much to clarify our conceptions by giving detailed clinical descriptions of the disorder, yet the methods ordinarily used to elucidate the pathology of physical disease, namely morbid anatomy and bacteriology proved inadequate in this sphere.

If progress were to be made, new conceptions were needed in order to understand and treat the schizophrenic disease process. Adolf Meyer (22)[x] takes the view that schizophrenia is the result of the progressive maladaptation of the patient to his environment. It is not a "disease" but a congeries of individual types of reaction, having certain general similarities. Although from the practical standpoint, Meyer believes that the subjective or psychological approach to the patient is the most

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[x] The numbers in brackets refer to the Bibliography.

effective in the early stages, yet he does not disregard anything which is of established value in the field of physical pathology.

After mentioning that physicians are now concerned, for instance, with early tuberculous infection instead of "consumption", he says, "In the same way, a knowledge of the pathological process in schizophrenia will put us in a position to regulate the patient's mental and physical habits, as long as dementia is merely potential and not an accomplished fact. To be sure, the conditions are not so simple as with an infectious process. The balancing of mental activity and its influence on the autonomic nervous mechanisms can miscarry in many ways."

The passage just quoted speaks for a more careful study of physiological changes in the early stages of chronic mental disorder. This being so, there are reasons for directing attention particularly to the respiratory system. While it has long been known that changes in breathing are closely related to mental changes, certain recent experiments with carbon dioxide have shown what striking effects can be produced on the patients in a catatonic stupor by the administration of this gas.

Scarcely any more striking experiment has been carried out in connection with schizophrenia, than that reported by Loevenhart, Lorenz and Waters in 1929 (19). They showed that mixtures of carbon dioxide and oxygen under certain circumstances produced a striking effect on catatonic stupor. Patients who for years had remained mute, became responsive to their environment for periods varying from two to twenty-five minutes. The mutism and muscular rigidity disappeared and they answered questions when addressed. The writer with C.P. Richter carried out one such experiment in 1930 at the Johns Hopkins Hospital, Baltimore.

The procedure as described by Loevenhart is as follows - The patient at first inhales a mixture containing 15 per cent of carbon dioxide and 85 per cent of oxygen. Within a minute or less, respiratory stimulation develops which is easily observed in the type of case selected, because normally the respiratory movements are quite shallow, slow and regular. They found, however, that a more marked response was invariably obtained if the carbon dioxide content of the mixture were increased. This should therefore be increased, but not by more than 5 per cent each minute, until a final concentration of 30-40 per cent is reached, the oxygen concentration being therefore 60 - 70 per cent.

The usual response of the patient to the administration of this mixture was as follows. The catatonic patient usually relaxed, and some spontaneous movements of the extremities occurred. The limbs became flaccid except in long standing cases where contractures had developed. Sweating also occurred. The patient gazed round him with dilated pupils. In most cases expiratory phonation was observed. A conversation was sometimes possible with the patient. Those patients having a smirk or silly grin, lost it, and those exhibiting an apathetic expression, changed to an animated expression, apparently characteristic of the individual. Muscular movements of the extremities were purposeful and adequate. This response might last 2-25 minutes or more in patients who had been previously markedly stuporous and wholly inaccessible.

Such striking changes in a serious mental condition were well worth further study. Conclusions, however, would be difficult to draw as long as human subjects were employed, for it remained doubtful how far the changes could be explained as being caused specifically by the action of carbon dioxide. It seemed possible that they were merely caused by fright or some other psychological cause.

These workers were themselves doubtful how far the phenomena could be explained at the purely physiological level. They write: "The mental reaction, more especially the return to the stuporous state after a period of wakefulness, suggests seeking a refuge from reality, as though the world were a painful experience, and stupor and sleep preferable."

SCOPE of the PRESENT ENQUIRY.

The phenomena described above could be more exactly studied if the subject for experiment were a laboratory animal instead of a human being. If a macac monkey could be made cataleptic, and then subjected to various doses of carbon dioxide, changes in the direction of stimulation or depression of function could be more precisely studied. The phenomena could be investigated at the purely physiological level in the simpler organism of the monkey.

When the writer first helped carry out an experiment of the kind described above, he had already been engaged with C.P. Richter (30) on a method of studying the intensity and duration of the catalepsy produced in monkeys by bulbocapnine.

In what follows, an account is first of all given of the effects of varying doses of carbon dioxide on the intensity and duration of bulbocapnine catalepsy in monkeys, a condition which closely resembles that described above in man.

In addition, however, other problems were opened up. These authors commenting on the action of carbon dioxide wrote in the same article,

> "It is interesting to note the work of Golla, Mann and Marsh (8) in the light of our own study. These investigators have shown that in certain psychotic individuals there is a

marked reduction in the sensitivity of the respiratory centre to carbon dioxide. Our observations are in entire accord with this finding. Indeed, the decreased irritability of the cerebral cells to normal carbon dioxide content may be the crux of the psychotic state in question, since a sufficient increase in the carbon dioxide causes a restoration of what we regard as relatively normal psychic function."

The same writers also report that the respiration of the catatonic patients seemed shallow, slow and regular.

Such statements as these bring home to one how little is definitely known about the respiration of psychotic patients. This fact caused the present writer to embark on further studies which were closely related to the first. These further observations comprise the second and third sections of the thesis. In them are reported the results of experiments conducted at the laboratories of the Maudsley and Colney Hatch hospitals, London. The second section concerns the amount of air breathed by catatonics and others, and whether their type of respiration differed from the normal in respect of depth and rate. In the third section, other abnormalities, especially connected with respiratory rhythm, are discussed.

SECTION I.

THE EFFECTS OF CARBON DIOXIDE INHALATION ON EXPERIMENTAL CATALEPSY IN MONKEYS.

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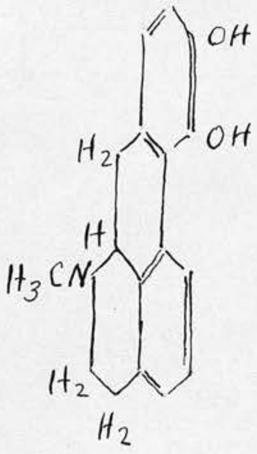
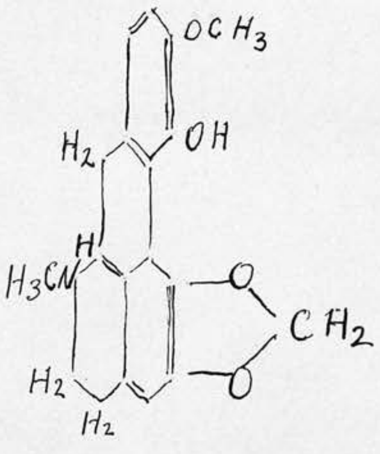
Catalepsy may be defined as a condition in which the individual tends to maintain an attitude however awkward for an indefinite period. It is to be distinguished from paralysis in that the individual may under certain circumstances be induced to move the limbs, but immediately thereafter continues to hold himself indefinitely in another posture. The chief importance of catalepsy from the medical point of view lies in the fact already mentioned that it is a symptom which is found in the catatonic form of schizophrenia. Catalepsy, however, is only one of the symptoms of catatonia. It may also be characterised by negativism, automatic mimicry of action or speech, impulsive movements, grimaces, sudden periods of excitement; also by certain symptoms relating to the autonomic nervous system, such as salivation, vomiting, sweating, incontinence of urine. The respiration is shallow.

It was demonstrated by Peters (24) in 1904 that the injection of moderate doses of bulbocapnine was capable of producing in animals a condition of great inactivity and catalepsy. These do not move except when urged or prodded, and they maintain difficult and awkward postures for long periods of time. Bulbocapnine is an alkaloid obtained from the plant Corydalis Cava. Its formula shows some similarity to that of apomorphine. It was worked out by Gadamer and Kuntze[x] (13).



Apomorphine.



Bulbocapnine.

It has been a matter for controversy how far the symptoms produced by this drug are comparable

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[x] Arch der Pharmazie 1902 quoted by de Jong and Baruk (13) p. 15.

to those found in the catatonic form of schizophrenia. De Jong and Baruk, in their book, "La Catatonie Expérimentale" p. 125 write:-

"Nous avons montré que la bulbocapnine peut reproduire chez l'animal un état superposable dans tous ses détails à la catatonie humaine, c'est-à-dire non seulement la catalepsie qui, nous le répétons, n'est qu'un symptôme nullement caractéristique à lui seul de la catatonie, mais encore le négativisme, les hyperkinésies (stéréotypies, impulsions, maniérisme) et des troubles organo-végétatifs."

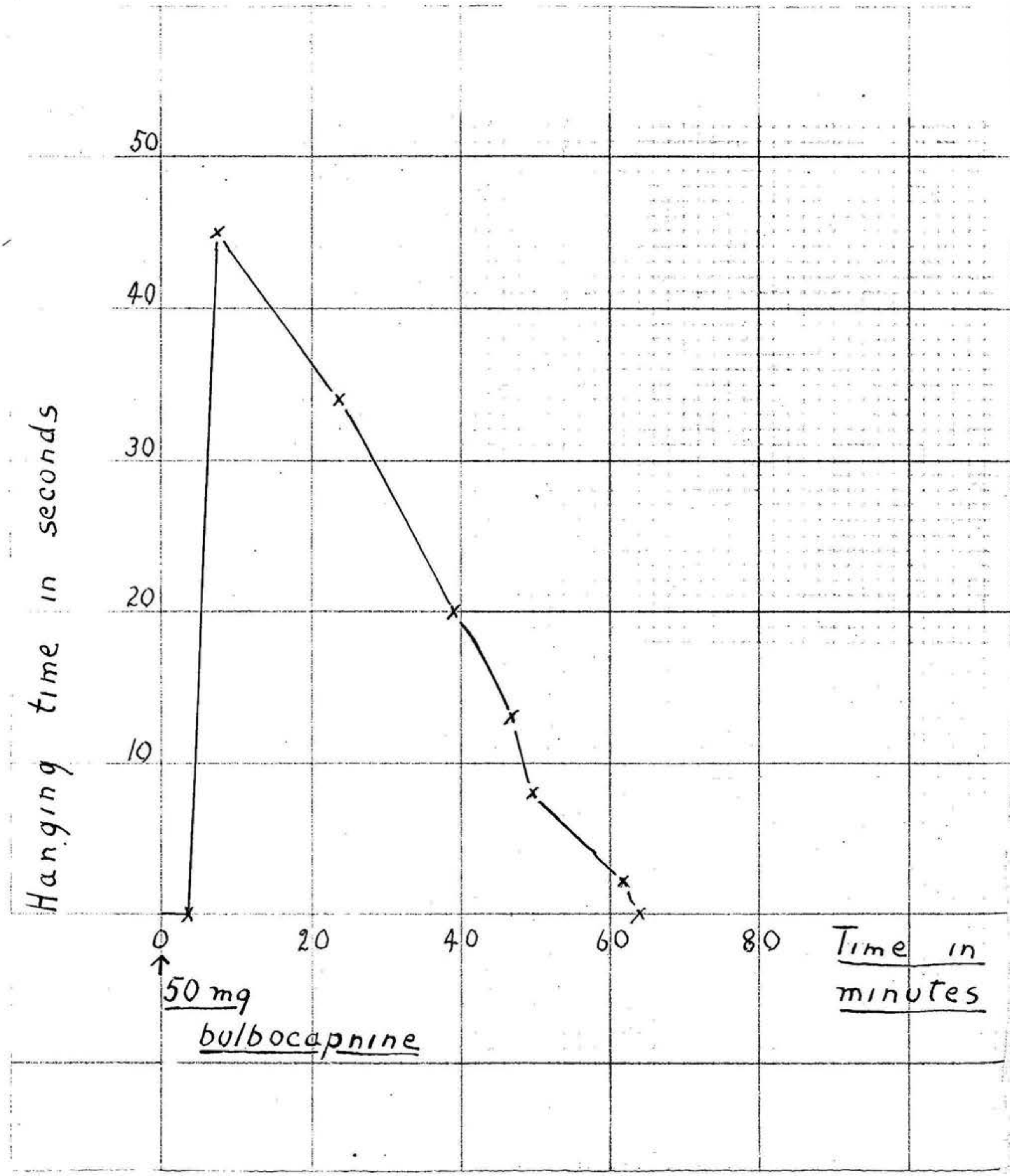
It must be pointed out, however, that not every investigator has so equated the symptoms of bulbocapnine poisoning with those of catatonia. Some writers, e.g. Divry,(5) have pointed out resemblances to the Parkinsonian syndrome, noticeably in the tremor which occurs, especially in monkeys. The truth in the present writer's opinion is that the symptoms of bulbocapnine poisoning are not absolutely identical with those of catatonia in man. Nevertheless, the catalepsy together with the autonomic nervous symptoms produces a picture sufficiently near, to justify conclusions being drawn from the action of drugs such as carbon dioxide upon it.

The present writer in collaboration with C.P. Richter (29), devised a method for measuring the depth and duration of catalepsy in the monkey. This was by means of a "hanging reflex" which was present during the catalepsy. Catalepsy has already been defined as the tendency on the part of the individual to maintain an awkward attitude indefinitely. The degree of the catalepsy was measured by the length of time during which the monkey would maintain one particular position, namely hanging from a bar with one hand when the other three limbs were tied together. (See accompanying photograph, Fig. 1). The length of time between the monkey first holding on to the bar and finally dropping into the net could be measured exactly. If the monkey were made to hang by one hand at intervals after the injection of bulbocapnine, the length of time that it remained suspended at each hanging became less and less until the hanging response disappeared with the catalepsy. The fact that the monkey hung

Fig 1.

See page 12.

Chart 1.



See p. 13.

for a shorter and shorter period at each hanging was not caused by mere fatigue. A monkey, hung for the first time an hour after injection, remained suspended just as few seconds as a monkey which had been hung at intervals since the injection. In this way charts could be made (Chart I.) of the effect of bulbocapnine, the ordinates showing the degree of catalepsy and the abscissae the duration of the effect of the drug.

It was found empirically that this hanging response was only present with doses of bulbocapnine sufficiently great to produce catalepsy, and disappeared again with the larger doses which produced over-activity and convulsions.

It may be remarked that F.M.R. Walshe and E. Graeme Robertson (32) consider that this hanging response described by us has little to do with the "grasp reflex" which is present in cases of certain tumours of the cerebral hemispheres. They consider the hanging response to be a reflex elicited by stretch in certain conditions of increased muscle tone.

DESCRIPTION OF THE METHOD.

The apparatus used in the present study and the method of hanging the animals is shown in the photograph. The horizontal brass bar from which the animals hang is three eighths of an inch in diameter, and is fastened to two stands, about three and a half feet above a net in which the animals are caught when they fall.

In order to hang the monkeys by one hand at a time, it was necessary to tie the two legs and one arm together, because otherwise the animals invariably pulled themselves up on a bar and held on with both feet and hands. The normal procedure was to tie a strip of muslin bandage about three feet long round one leg just above the ankle joint; then round the other leg with a double loop and knot. It is important to tie each foot and hand separately in this way, for otherwise the monkey is able to escape from the bandage very easily and upset the readings.

After the two legs and one arm are tied together, the animal is grasped by the head and lifted in the direction of the bar until the palm of the free hand comes in contact with the bar, and the animal is able to obtain a firm hold. The animal is then gently released. The time that it hangs before it falls into the net is measured with a stop watch. It is important to call attention again to the fact that a normal monkey not under the influence of bulbocapnine refuses to hang, drops at once into the net, and attempts to run away. For the sake of clearness most of the charts show the record of the right hand only.

The bulbocapnine was injected in doses which had previously been found to give the greatest degree of catalepsy. This was about 17 mg. per Kg. of body weight, injected subcutaneously.

The carbon dioxide was given with a mask in concentrations varying from 15 to 50 per cent over periods of from one to six minutes.

Several curves with moderate doses of bulbocapnine alone were obtained from each animal before bulbocapnine in combination with carbon dioxide was administered. For the most part the carbon dioxide was given some time after the peak of the effect produced by bulbocapnine was reached, and the times during which it remained suspended had become shorter.

Observations were made at the same time of changes produced by the carbon dioxide on the general behaviour of the animal, with special attention to the changes produced on its responsiveness, as an index of any modification in the degree of catalepsy.

RESULTS OF EXPERIMENTS.

1. Effect of Carbon Dioxide on Bulbocapnine Catalepsy.

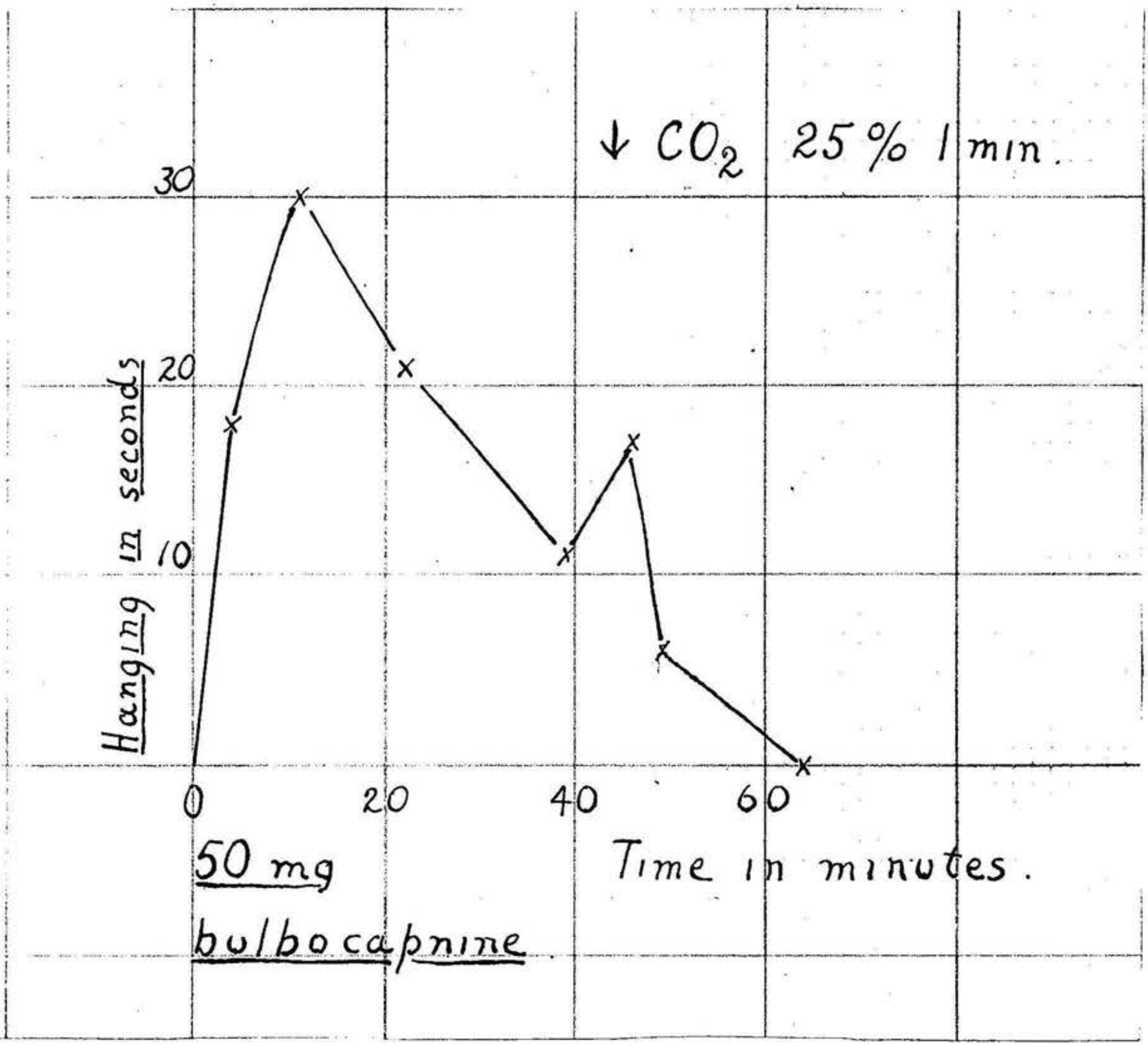
Carbon dioxide was administered on 18 occasions to monkeys which had already been made cataleptic by bulbocapnine, and on 40 occasions to normal monkeys to which no bulbocapnine had previously been given.

EFFECT ON THE HANGING RESPONSE.

Where carbon dioxide was given to monkeys already injected with bulbocapnine it was generally administered about 40 - 60 minutes after the injection of bulbocapnine, when the effect of the bulbocapnine was no longer maximal.

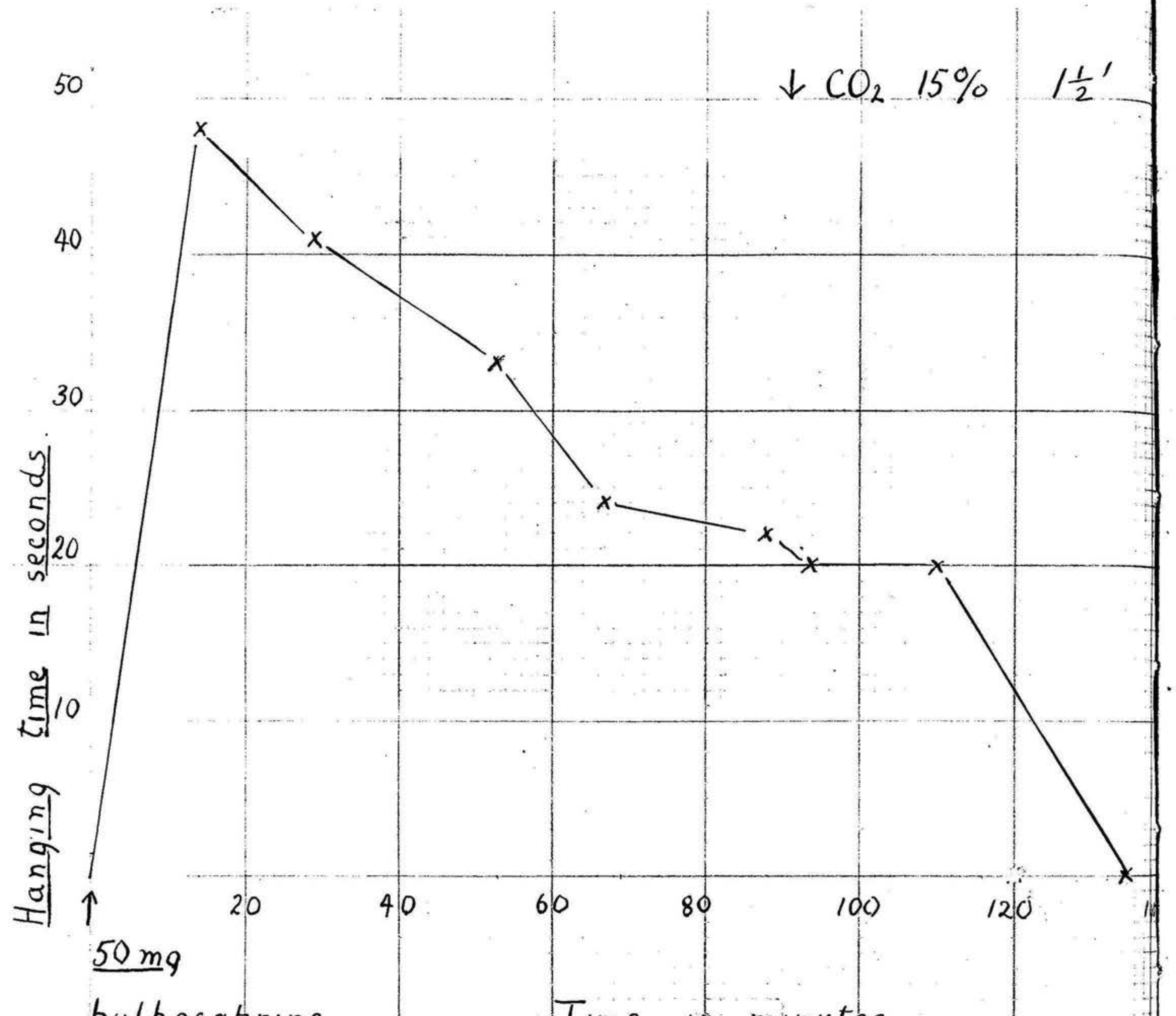
The carbon dioxide was given in varying doses. These will be classed as follows:-

Chart 3.



See page 17.

Chart 2. (Chart 3 on preceeding page)



See page 17.

(1) 15 per cent.

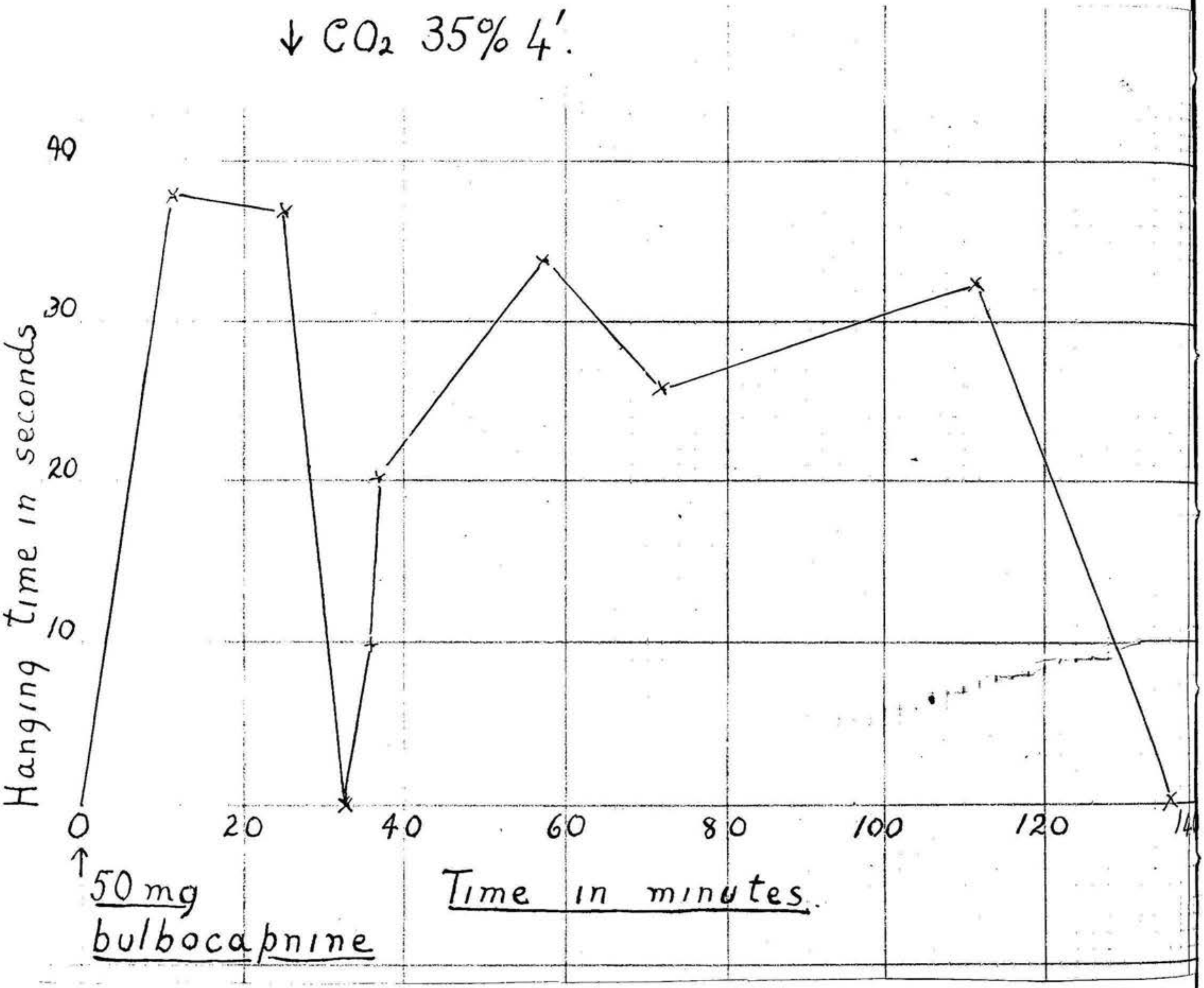
(2) 25 per cent.

(3) 35 per cent and over. (See Table I.)*

In two records taken with 15 per cent carbon dioxide no effect was produced on the bulbocapnine curve. Chart 2 shows a curve obtained from a monkey injected with bulbocapnine. Fifteen per cent carbon dioxide was administered, as shown, but no marked effect was produced on the curve. Twenty five per cent carbon dioxide was also administered on seven occasions to monkeys for $1\frac{1}{2}$ to 3 minutes. In every one of these cases, there was an immediate increase in the catalepsy as measured by the hanging response. (Table I.)+ Chart 3 shows one of these. The hanging response had appeared after an injection of 50 mg. of bulbocapnine, had reached a peak and begun a gradual decline. The carbon dioxide given 44 minutes after this dose of bulbocapnine, caused a temporary increase in the hanging time, from eleven to seventeen seconds. The curve then resumed its original course and the response disappeared completely 64 minutes after the initial injection of bulbocapnine.

* Inserted at end of book.

Chart 4.



See page 18.

The animal whose curve is shown in Chart 4 received a higher concentration of carbon dioxide, 35 per cent for 4 minutes, 26 minutes after the initial injection of bulbocapnine. It will be noted that this caused an instantaneous disappearance of the hanging response. It returned within a minute however, reached a level almost as high as before, and persisted for some time, so that the total duration of the effect of bulbocapnine was markedly prolonged beyond its average length (136 minutes as compared with 66 minutes which was the average for that monkey).

Curves taken in the same way with doses of 40 and 50 per cent of carbon dioxide, showed, with 60 - 50 per cent oxygen, the same effect, if administered some time after the bulbocapnine. There was abolition of the response followed by augmentation.

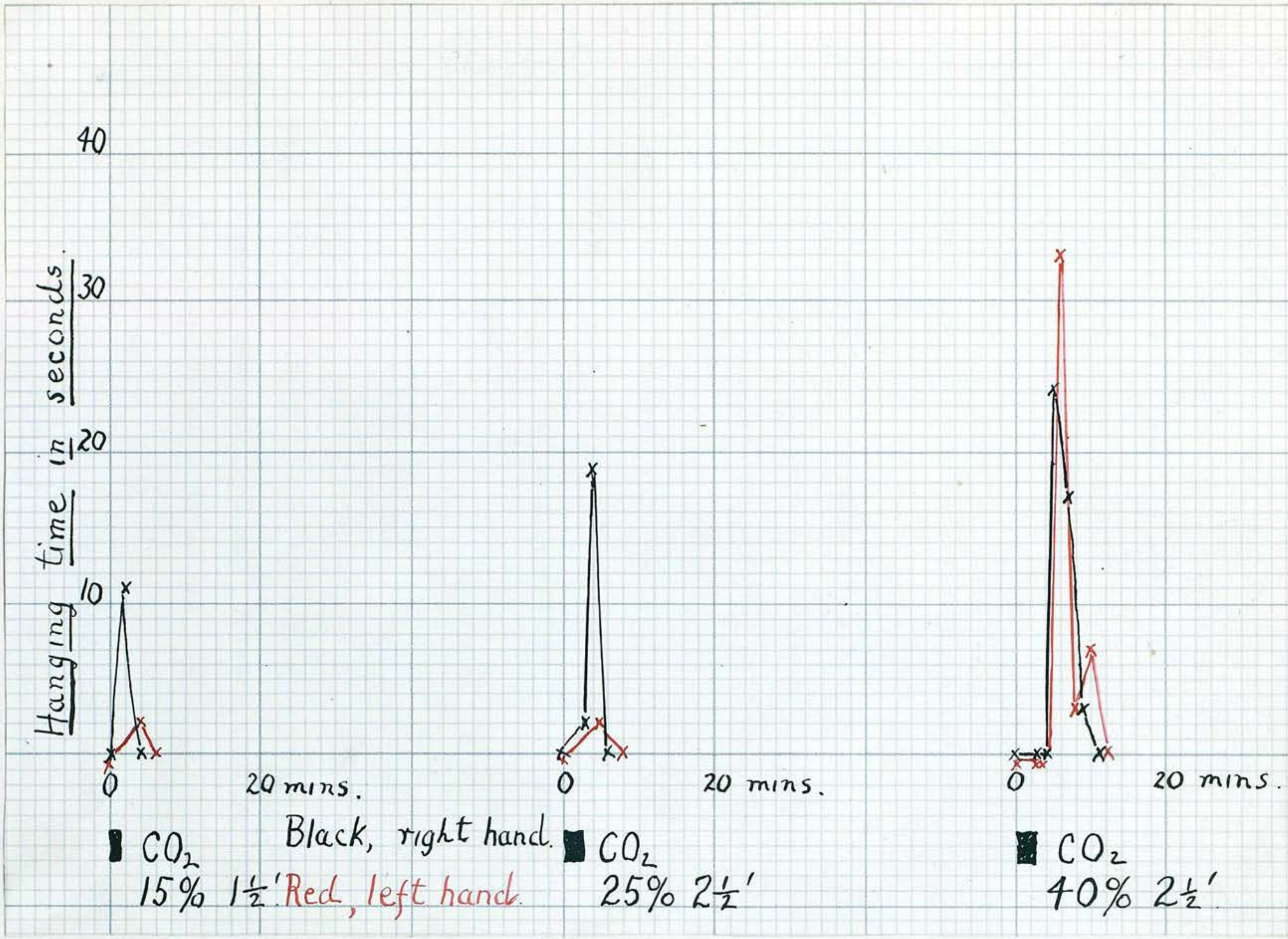
EFFECT ON GENERAL BEHAVIOUR.

Administration of carbon dioxide caused a profound change in the behaviour of the animals. Even before the mask was removed, they began to struggle and screech. For a few seconds afterwards, they sat still and looked as though dazed. Then quite suddenly they would come into full contact with their surroundings, leap from the table and attempt to escape. Within a few minutes as a rule they began to slow down, became less responsive and finally sank back into the original stuporous state. Kaufmann and Spiegel (16) have made similar observations on the effect of carbon dioxide on cats under the influence of bulbocapnine. The effect produced on cats, however, is less striking and less constant. This must be due in part at least to the lack of overt behaviour in the cat as compared to the monkey.

2. The Effect of Carbon Dioxide on Normal Monkeys not made cataleptic by Bulbocapnine.

It has been shown then that the effect of bulbocapnine, as measured by the hanging response, can be intensified by moderate doses of carbon dioxide. This paradoxical result suggested that carbon dioxide by itself might produce the hanging response. In order to test this the gas was administered to 5 monkeys in concentrations of 15 per cent., 25 per cent and 40 per cent. (See

Chart 5.



See page 20.

Table II.[+]) The time during which the gas was administered varied from $1\frac{1}{2}$ - 6 minutes. In two monkeys out of the five the hanging response appeared when 15 per cent was given for $1\frac{1}{2}$ minutes. The reflex was only just present and for a few seconds. In the third monkey it appeared when 15 per cent was given for 6 minutes, in the fourth when 25 per cent was given for $1\frac{1}{2}$ minutes, while the fifth required the same percentage for $2\frac{1}{2}$ minutes to bring out the response.

In all five monkeys the response was strongly present immediately after administration of 25 per cent, and might last for several minutes. The height of the curve was about the same as with bulbocapnine, but the length was much shorter.

With administration of 40 per cent carbon dioxide, however, there was a different effect of the gas on all five monkeys. In each case the monkey refused to hang for the space of half to one minute immediately after administration of the gas. Thereafter, however, the response was present, sometimes for as long as 20 - 40 minutes. A record of different doses given to the same monkey is shown in Chart 5.

+ Inserted at end of book.

EFFECT OF CARBON DIOXIDE ON BEHAVIOUR.

The animals seemed to be dazed while hanging under the influence of carbon dioxide, but their behaviour was different from that produced by bulbocapnine. They were more active, looked about blankly and bit the bandages securing their feet. There was a considerable amount of screeching and grinding of the teeth.

COMPARISON OF THE ACTION OF CARBON DIOXIDE ON MUSCLE TONE WITH THAT OF BULBOCAPNINE.

The action of bulbocapnine in producing cataleptic phenomena is only obtained by employing an intermediate dose of the drug. Larger doses produce hyperkinetic phenomena while smaller doses produce a state of somnolence. C.P. Richter and the present writer (29) summed up the matter as follows:-

"Doses of 7 to 8 mg. per kilogram body weight do not elicit the hanging response. The response appears with doses of 9 mg. or more. With larger doses up to 17 mg., the maximum strength of the hanging response and its total duration show a proportionate increase. With doses above 17 mg. the total duration of the effect continues to increase, but the maximum hanging time remains the same. In other words, the maximum hanging time is attained with doses of 17 mgm. and an increase in the dose will not make the animal hang longer in any one test. In adult monkeys this maximum hanging time is 30 - 60 seconds.

Doses of 40 mg. per Kg. B.W. and above, produce hyperkinetic phenomena lasting as long as 40 minutes after the injection, during which time the animal refuses to hang. Afterwards the response appears and persists usually for several hours."

If we consider solely the subject of muscle tone, we will see that carbon dioxide resembles bulbocapnine in that moderate doses, i.e. about 25 per cent, increase the tone, while larger doses (35 - 50 per cent) at first decrease tone so that the hanging reflex cannot be elicited, but later increase it.

The action of carbon dioxide therefore on the muscle tone of monkeys poisoned by bulbocapnine will vary according to the amount of bulbo-

Chart 6.

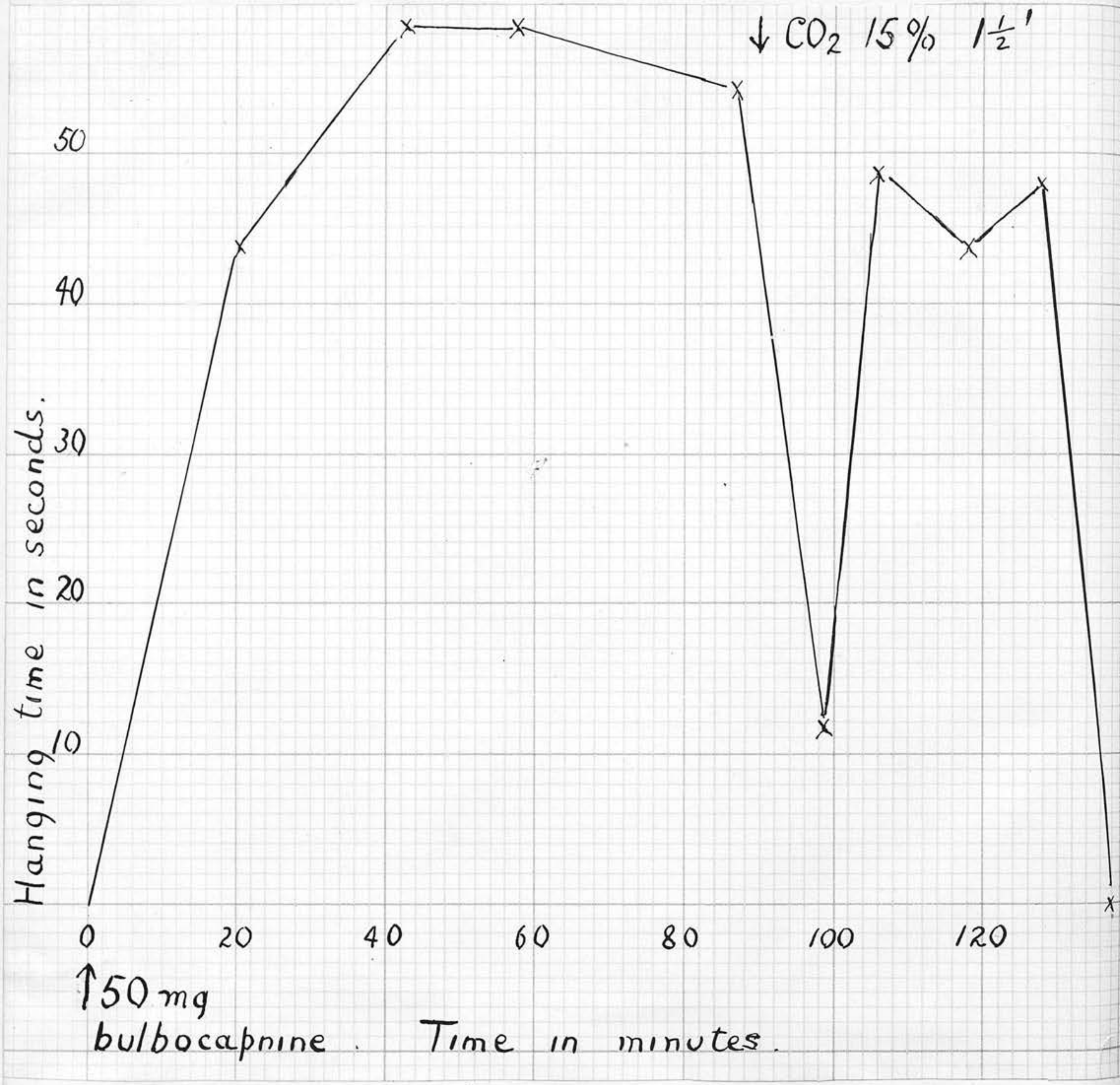


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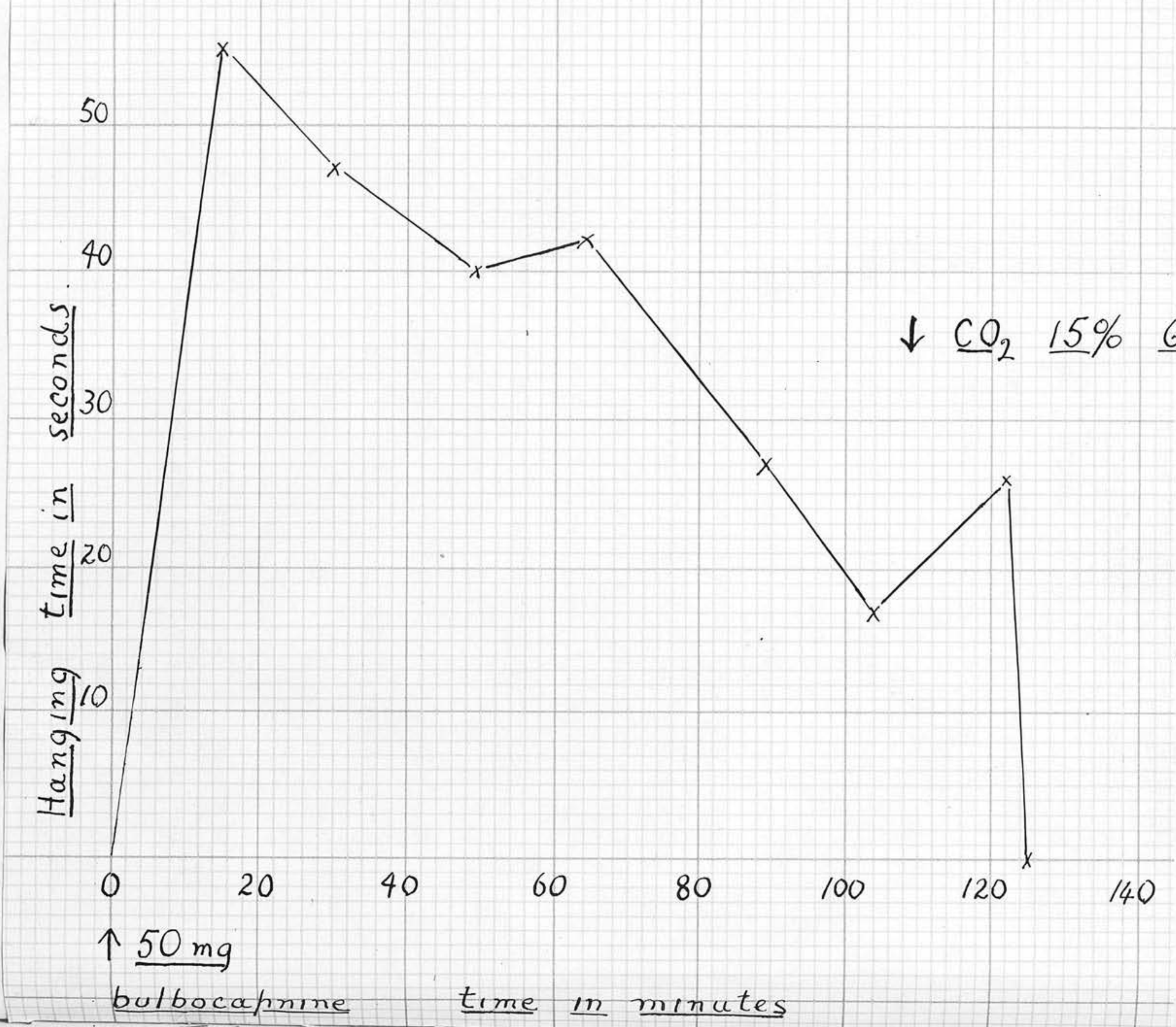
Chart 7.


60
50
40
30
20
10
Hanging time in seconds
↓ CO_2 15% 6'
0
20
40
60
80
100
120
140
↑ 50 mg
bulbocapnine
time in minutes

capnine already injected as well as the amount of carbon dioxide administered. If the monkey is already exhibiting the maximum hanging response through bulbocapnine, then comparatively little carbon dioxide will have the effect of at once abolishing or almost abolishing the catalepsy, just as if more bulbocapnine had been administered. This explains Chart 6, where 15 per cent for $1\frac{1}{2}$ minutes almost abolished the reflex, the response being already maximal with bulbocapnine. On the other hand in the same monkey (Chart 7) 15 per cent for 6 minutes brought back the reflex strongly just as it was disappearing after bulbocapnine.

Nevertheless where the hanging time is no longer maximal, that is, about three quarters of an hour after the administration of 17 mg. per Kg. of bulbocapnine, the effects of carbon dioxide are consistent. A dose of twenty five per cent causes an immediate increase of the catalepsy as measured by the hanging response, while larger doses first abolish it and later augment it.

TABLE III.

(See "Discussion" infra).

Showing the cerebral symptoms accompanying the phases preceding, during, and after the cataleptic state, with increasing doses of bulbocapnine, carbon dioxide and amytal.

Drug	Pre-cataleptic state produced by small dose. Hanging Response absent.	Cataleptic state moderate dose. Hanging response Present.	Ultra-cataleptic state large dose. Hanging Response Absent.
Bulbocapnine	Drowsiness	Stupor	Over-activity. Sudden impulsive movements; Occasional fits.
Carbon dioxide	Active	Active. Grinding teeth. Chattering. Squeaks.	Drowsy. Sleep. Occasionally convulsive movements, with high concentrations for many minutes.
Amytal	Active	Active but slightly dazed.	Asleep.

Note re Table.

The monkey which has been made cataleptic by a moderate dose of bulbocapnine resembles a human catatonic. When such a monkey is given carbon dioxide or amytal in large doses, it passes into the ultra-cataleptic state, just as if it had been given a higher dose of bulbocapnine. The mental condition however is no longer the same as if bulbocapnine alone had been given, but results from the combined effects of the two drugs.

DISCUSSION.

It may be remarked at this point that catalepsy is a condition which occurs as a reaction of the nervous system more commonly than is generally supposed. This fact has recently been emphasised by de Jong (14). Like the epileptic convulsion, it can occur as the result of disease or of intoxication by certain drugs. When it is caused by a drug, the amount of the dose must be, as we have seen, between certain limits. In the case of bulbocapnine for instance, this was between 10 and 30 mg. per Kg. Body Weight. A smaller dose merely causes drowsiness, while a larger dose causes a state of overactivity.

It is important when observing the effect of a drug on muscle tone to pay attention to the subject's behaviour and the degree of cerebral excitement. Table III. shows the degree of apathy or excitement which accompanies the precataleptic, the cataleptic and the ultra-cataleptic states of three different drugs, when given in increasing doses. In the case of bulbocapnine, the pre-cataleptic state of the animal is one of drowsiness, the cataleptic is one of stupor, while the ultra-cataleptic state is characterised by over-activity, with sudden impulsive and violent movements, or occasionally by convulsions.

Reference has already been made to the similarity of the cataleptic state caused by moderate doses of bulbocapnine to that found in human catatonia. The state of muscle, the stupor, and the autonomic nervous symptoms are very similar. The action of carbon dioxide on the human catatonic, as described by Loevenhart Lorenz and Waters, is almost identical to that observed on bulbocapnine monkeys. The limbs become flaccid, and the skin becomes moist. The staring eyes begin to move in a purposeful manner. The "expiratory phonation" is represented in the monkey by chattering and squeaks. The description of the return to the cataleptic state applies also to the monkey. The patient no longer responds to his environment, the eye movements cease, and "it is especially striking to note how completely the former muscular state is resumed."

When we come to analyse the effect of carbon dioxide on bulbocapnine catalepsy, we find paradoxically that the action on muscle tone is not antagonistic, but synergic with that of bulbocapnine. Carbon dioxide, like bulbocapnine, is one of those drugs which produce cataleptic phenomena in moderate doses, while failing to produce them in small or large doses.

Now, we have seen that if a monkey which has been made cataleptic by a moderate dose of bulbocapnine is given more bulbocapnine, it will come out of the catalepsy into the ultra-cataleptic and hyperkinetic state. In the same way if a monkey already showing the maximal cataleptic response is given a little carbon dioxide, it will pass temporarily into the ultra-cataleptic state, (Chart 6), just as if more bulbocapnine had been administered. Further, just as an additional dose of bulbocapnine to a cataleptic monkey is followed in succession by an ultra-cataleptic phase and then a phase of prolonged catalepsy, so the addition of carbon dioxide is followed not only by a non-cataleptic phase but also by a period of prolonged and usually intensified catalepsy.

Although in the matter of muscle tone the action of carbon dioxide is similar to that of bulbocapnine, in that it produces catalepsy[x] in moderate doses, yet the action on the cerebral centres and on behaviour is not the same. Reference to Table III. brings out this fact. Although catalepsy is accompanied by stupor both in bulbocapnine monkeys and in human catatonia, this is not necessarily so in animals rendered cataleptic by other means. With carbon dioxide the cataleptic state is accompanied by a considerable degree of cerebral activity, while the ultra-cataleptic state is one of drowsiness. Similarly with amytal, to which reference will be made later, the cataleptic state is accompanied by some degree of cerebral activity while the ultra-cataleptic state is characterised by sleep.

If an animal is in a state of catalepsy, it

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[x] "Catalepsy" is used here in the sense of increased muscle tone, so that the hanging response is present. De Jong has described "experimental catatonia" produced by carbon dioxide. Ztschr. f.d. ges. Neur. u. Psychiat. 1932 CXXIX. 25 ff.
De Jong however did not give oxygen with CO_2 and therefore his results as far as they go might be due to ~~asphyxia.~~ anoxaemia.

may be brought out of it either by withdrawing the poison so as to put it into the pre-cataleptic state, or by increasing the dose until the animal is in the ultra-cataleptic state.

It will be noticed from Table III. that the ultra-cataleptic state in bulbocapnine poisoning resembles catatonic excitement, with its sudden uncontrolled movements. The resemblance was emphasised by de Jong and Baruk.[x] With carbon dioxide on the other hand, the cataleptic state is accompanied by behaviour suggesting active thought, while the ultra-cataleptic state is one of drowsiness. When the bulbocapnine catalepsy is interrupted by carbon dioxide, the usual effect is as follows. The catalepsy first becomes maximal, and then the animal passes into the ultra-cataleptic phase, not the more normal or pre-cataleptic phase, as might have been supposed if the drug had been antagonistic in its

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[x]Op cit page 89. "Ces hyperkinésies, nous l'avons vue, sont provoqués en général par des doses de bulbocapnine plus élevées que celles qui réalisent la catalepsie et la négativisme .... Ces faits rappellent exactement les impulsions si speciales et si fréquentes des catatoniques qui présentent le même caractère de brusquerie, de brièveté, et de début inattendue."

action to bulbocapnine. An illusion of normality is given because the excitement of the ultra-cataleptic state of bulbocapnine poisoning is counteracted by the depressant effect of large doses of carbon dioxide. Before the animal can become normal, it has to pass a second time through the cataleptic state. This is shown on the hanging charts by the maintenance or increase of the catalepsy following its abolition.

That bulbocapnine catalepsy closely resembles that found in human catatonia is given support by recent work of Giacomo.(6) Human catatonics when given bulbocapnine behaved in a manner very similar to animals already made mildly cataleptic by bulbocapnine. Giacomo injected 200 mg. intravenously into a number of psychotic subjects. (The dose injected was a relatively small one compared to that injected into monkeys. Nevertheless Giacomo claims that the intravenous route is more effective than the subcutaneous.) Twenty four experiments were carried out on 16 subjects (eight schizophrenics and eight epileptics or feeble-minded). There was an undoubted increase of catalepsy in two schizophrenics, and a doubtful increase in three other schizophrenics. There was observed an intense catalepsy in two feeble-minded and a slight catalepsy in two others. In two subjects, however, bulbocapnine produced a short confusional crisis with intense psychomotor excitement.

If we suppose that the state of catatonic excitement in man corresponds to the ultra-cataleptic state produced by large doses of bulbocapnine, as stated by de Jong and Baruk, then the results obtained by Giacomo are readily explained. The administration of bulbocapnine caused in some individuals an increase in the cataleptic state, but in others, where the degree of catalepsy was already maximal, the hyperkinetic symptoms of the ultra-cataleptic state were produced.

This conception of human catalepsy would also explain the action on it of the drug known as amytal. Its effect on muscle tone is similar to that of carbon dioxide. It has also been used to interrupt catatonic stupor in man.

This has been described by Bleckwenn (3) as follows:-

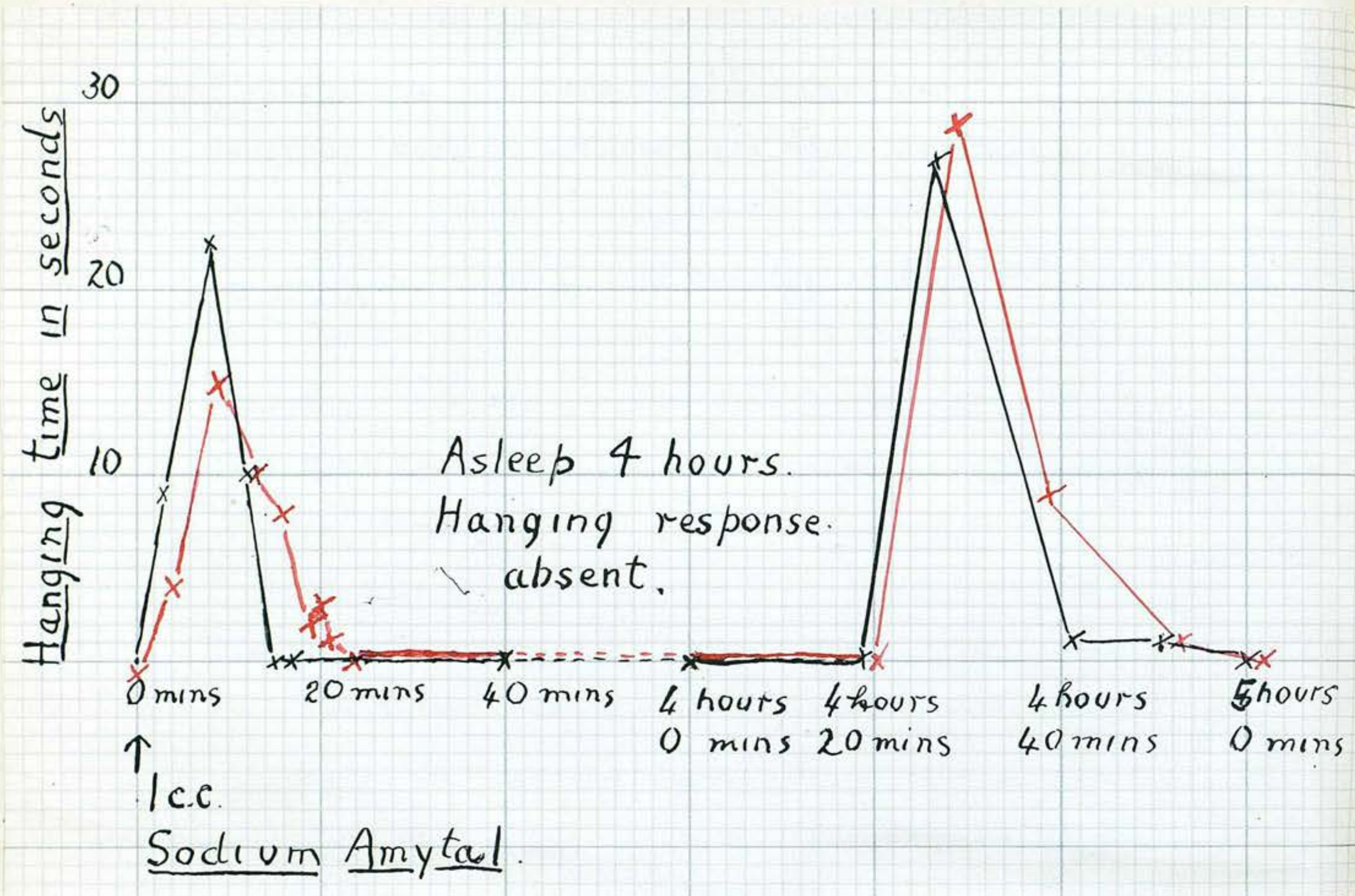
"Catatonic patients can be aroused from their

> stuporous states for intervals of from two to fourteen hours, during which, if previously tube-fed, they eat ravenously, show spontaneity, ask and answer questions with consistent emotional reactions."

The writer working with C.P. Richter (30) showed that this drug produces catalepsy in moderate doses. (Chart 8). It will be seen from the chart and also from Table III. that in the ultra-cataleptic state, the animal passes into a condition of sleep from which it becomes cataleptic a second time before ultimately becoming normal again. When amytal causes a catatonic patient to emerge from his catalepsy, the action is most easily explained by supposing that the patient passed into an ultra-cataleptic state where the tendency to catatonic excitement is counteracted by the soporific qualities of the drug, and that when these wear off, he then passes into a state of renewed catalepsy.

To come to the more practical application of our experiments, their object has been to discover why carbon dioxide appeared to abolish catalepsy both in human catatonics and in

Chart 8.



See page 32.

bulbocapnine monkeys. The state of muscle tone produced by carbon dioxide in these circumstances, so far from being more normal, was so far removed from the normal that the monkeys had again to become cataleptic before they could become normal.

Seeing that our next object is to apply a drug which will give the bulbocapnine monkey longer and longer respite from the catalepsy in the hope that the same drug will be effective in human catatonia, it would seem reasonable to give a drug which is not in itself capable of producing catalepsy; in other words a drug which is antagonistic to bulbocapnine not synergic with it, not only in regard to behaviour but to muscle tone as well. We should look for a drug which would change the catalepsy to the pre-cataleptic state, and not to the ultra-cataleptic state, as is the case with carbon dioxide.

A very significant fact, however, in connection with these experiments is that carbon dioxide, which is capable of causing and modifying the cataleptic state, is found naturally in the body. This fact has been emphasised by de Jong. (14). It points the way to a further investigation of the respiratory system in psychotics to see whether their type of respiration particularly in regard to carbon dioxide is in any way different from that of normals.

SECTION II.

THE DEPTH AND RATE OF RESPIRATION IN NORMAL AND PSYCHOTIC SUBJECTS.

SECTION II.

The depth and rate of respiration in normal and psychotic subjects.

It has frequently been remarked clinically that schizophrenic patients appear to breathe more shallowly than normal subjects. Very little, however, that is clear and indisputable has been written on this subject up to the present.

Two French writers, Mignot and Le Grand (23) gave a report in 1926. They do not state the numbers examined. Actually they give an account of the respiratory records taken by a pneumograph of 9 schizophrenic females. They state that the average frequency of respiration among normal women is 18 per minute. They say, however, that in almost all cases of dementia praecox that had disorders of phonation, the number of respirations was diminished to 8, 12, 15 per minute. This slowing was caused, most often, by an expiratory pause lasting 3, 5 or 7 seconds.

An Italian worker, S. Gullotta (1931) (10) again working with a pneumograph, in this case applied to the abdomen, stated that the frequency varied within the limits of the normal. It was less frequent in the records of catatonics, but more frequent in other cases of dementia praecox. With regard to the depth, it was clearly inferior to normal in all the cases examined. The exact recording of the depth, however, and also of the rhythm, has been attended by difficulties. Most observations described in the literature have been made by means of a stethograph, that is to say, a rubber tube of some kind fixed round the thorax or abdomen. As such an apparatus may direct the subject's attention to his breathing, the value of the results obtained may be vitiated. Moreover, such a method cannot record accurately the magnitude of each respiration. Another objection is that the stethograph is measuring only one part of the respiratory mechanism, and at any moment the respiration may change from thoracic to abdominal or vice versa. In the course of one of my experiments in which records of the thorax and abdomen were being made simultaneously, the movements of the abdomen became smaller and those of the thorax greater without altering the amount of air respired, as measured simultaneously by the plethysmograph. The excursion recorded therefore in one case by this method cannot be compared quantitatively with that recorded in another, nor even with the excursion in the same individual at a different time.

TECHNIQUE.

The apparatus described by Golla and Antonovitch (7) disposes of these difficulties. It is shown in the accompanying diagram. (Fig. 2). It consists essentially of a wooden box with a removable lid and front piece, both of which can be clamped firmly into position by means of a hand-screw. The subject for experiment sits in the box and only his head projects through a hole in the roof. The box is air-tight and the opening for the neck is occluded through the subject's wearing an inflatable rubber collar, to which an "apron" is attached all round. The latter is clamped between two boards in the roof of the box. These collars are made of varying sizes. The air space in the box communicates with the recording plethysmograph by a wide tube.

The recorder itself is of the simple float pattern, rectangular, and having a capacity of fig 2.

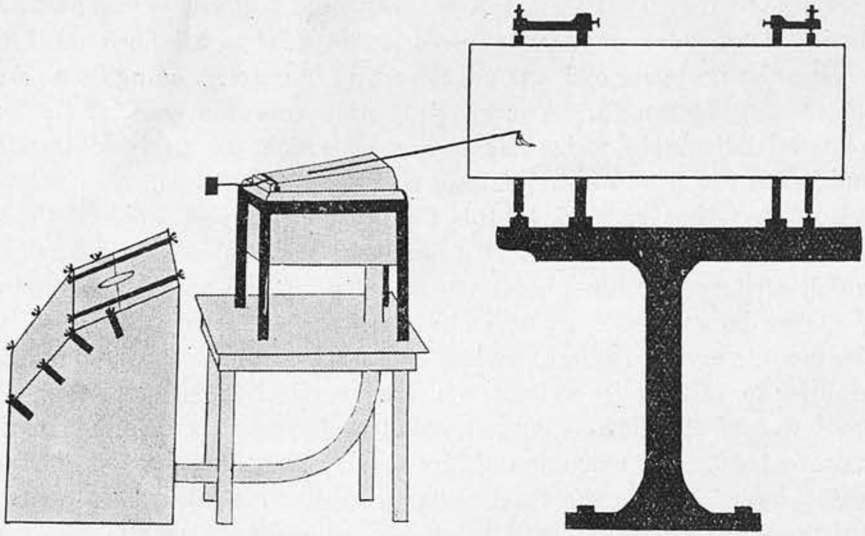


FIG. 1.—Sketch of apparatus.

See page 36.

about 4 litres. The float is balanced on knife edges at its posterior end, the edges resting in corresponding notches on the wall of the water bath.

Several precautions were taken to keep the conditions uniform throughout the experiments. No external stimuli were allowed to disturb the patient. He merely sat quietly in the box, and was unable to see any of the recording apparatus. He was unaware that his respiration was being examined. His attention was therefore not directed towards his respiratory movements, a circumstance which would <u>ipso facto</u> have rendered the results less valuable. Factors which might interfere with the processes of metabolism were kept uniform. The subject sat still until he had become accustomed to his environment. If he was obviously alarmed, which in fact seldom occurred, the experiment was abandoned. No record was taken after the subject had been active physically, or soon after a meal. A minimum of clothing was employed in order to prevent undue warmth inside the box.

RESULTS.

The accompanying table shows the results of these investigations. In this series 217 subjects were examined, including 44 normal men and 18 normal women. The normal subjects were members of the staffs of the Maudsley and Colney Hatch Hospitals. 85 schizophrenic males and 36 schizophrenic females were examined. Most of these were suffering from a considerable degree of dementia. By way of comparison, 6 males and 19 females who were melancholic but not demented were examined.

TABLE IV.

Number	Class	Mean area of body surface in sq. metres	Mean vol. of tidal air in c.c.	Mean rate of respirations per min.	Mean vol. of respirations per min. in litres
	MALES.				
44	Normals	1.815 ± .012	572	16.77 ± .329	9.59
85	Schizophrenics	1.592 ± .008	442	19.61 ± .293	8.67
6	Melancholics	1.630	623	18.67	11.65
	FEMALES.				
18	Normals	1.578 ± .016	429	18.61 ± .494	7.98
36	Schizophrenics	1.509 ± .020	339	22.67 ± .363	7.68
19	Melancholics	1.517 ± .020	402	19.55 ± .685	7.86
8	Normals (dozing state	1.578	491	13.50	6.62
8	Normals (sleeping state)	1.578	317	15.00	4.76

When one compares the amount of air respired as between two groups, the size of the subjects must be taken into consideration. One would expect a large individual to breathe more deeply than a small one. The factor used by physiologists to make possible a comparison of the oxygen consumption of two individuals of different size is the area of body surface, and this has been used in the present study. It was calculated from the height and weight of each patient by means of Boothby and Sandiford's nomograph. (29) The mean size of each group is shown in the first column in square metres of area of body surface. The second column shows the mean volume of the tidal air of each group measured in cubic centimetres. The third column shows the mean number of respirations per minute for each group. When this is multiplied by the figure giving the tidal air we obtain the volume of air breathed per minute, here given in litres in the fourth column.

Looking at the volume of air respired (tidal air) as recorded in the second column, one finds that the figure for normal males is a little higher than that usually given in text-books for subjects at rest. The usual figure is 500, but the present figure is 572. The reason for this is that the subject was sitting, not lying, and that the temperature inside the box was rather higher than normal.

In order to allow for the fact of difference in size, the mean size of each group, (normals, schizophrenics, and female melancholics) was calculated. The probable error and standard deviation were worked out together with the correlation coefficient of volume of respiration with area of body surface.

TABLE V.

Area of Body Surface in Square Metres.

	Mean	Standard deviation
MALES		
Normals	1.815 ± 0.012	0.1138
Schizophrenics	1.592 ± 0.008	0.1153
FEMALES		
Normals	1.578 ± 0.016	0.1021
Schizophrenics	1.509 ± 0.015	0.1372
Melancholics	1.517 ± 0.020	0.1315

COMPARISON OF SIZE OF NORMALS AND SCHIZOPHRENICS - It will be noticed in Table V. that the mean area of body surface of male schizophrenics (1.592) is very much smaller than that of normals (1.815), the difference being significant. For females the schizophrenics have a mean area which is smaller than for normals to an extent which is just significant, the difference being three times the probable error (0.069 ± 0.02).

TABLE VI.

Volume of Tidal Air in Relation to Size of Subject.

	Volume of tidal air in c.c.	Standard deviation	Correlation coefficient with area of body surface.
MALES.			
Normals	572	143	r = + 0.2216
Schizophrenics	442	79	r = + 0.1096
FEMALES.			
Normals	429	74	(Too few cases)
Schizophrenics	339	52	r = - 0.0419
Melancholics	402	57	(Too few cases)

For males, the schizophrenics have a much smaller mean volume of tidal air and also a variability which is much less than for normals. Part of the difference in the means results from their smaller size, but this can be taken into account since the correlation of volume of tidal air with area of body surface is known. The volume of tidal air which normal subjects with an area of body surface of 1.592 square metres would be expected to have is 510 c.c. Actually, the male schizophrenics had a mean volume of 442 c.c. Hence the difference between the actual and expected is 68 c.c. As its probable error is $\pm$ 15.6 c.c., the difference is more than four times its probable error after correction for difference in size, and is therefore significant.

For females there is no sensible correlation between volume of tidal air and area of body surface, and therefore there is no need to correct for the slight difference in mean area of body surface. The mean volumes may therefore be compared as they stand. For female schizophrenics the difference from normals is 90 $\pm$ 13.0 c.c. Since the difference is about seven times its probable error, it is certainly significant.

RATE OF RESPIRATION. Since there is no correlation between rate of respiration and area of body surface, there is no need to correct for difference in area of body surface. For males the rate for normals (see Table IV.) was 16.77 ± 0.329, and for schizophrenics 19.61 ± 0.293. The difference is 2.83 ± 0.441, which is six times its probable error, and is therefore certainly significant.

For females, the normals show a rate of 18.61 ± 0.494, while that of schizophrenics is 22.67 ± 0.363, a difference of 4.06 ± 0.613. Since the difference is over six times the probable error, it is again certainly significant.

From these results, then, it appears that schizophrenics on the average breathe more shallowly and more rapidly than normals.

MELANCHOLICS. Nineteen female melancholics were found to have an area of body surface which was smaller than that of normal females (Table IV.) The smaller size, however, was barely significant. The volume of tidal air was smaller than that of normal females, but the difference (27 ± 14.70 cc.) was also not significant.

Regarding their rate of respiration, for 19 female melancholics this was 19.55 ± 0.685 as against 18.61 ± 0.494 for normal females. This difference was not significant.

It would appear, therefore, that the difference in volume and rate of respiration in schizophrenics does not apply to melancholics. The number of male melancholics (6) was too small to give significant results. These on the average breathed more deeply and rapidly than normals (Table IV.)

COMPARISON OF SCHIZOPHRENICS WITH NORMAL SUBJECTS IN A DOZING AND SLEEPING STATE. In the last two lines of Table IV. figures are given showing the respiratory depth and rate of normal women first in a dozing and secondly in a sleeping state, in order to show the difference from schizophrenics. In these experiments the subject was lying in a chest made on the same principle as the box described above. I am indebted to Dr. Antonovitch for these records. It will be seen that in the dozing state the breathing is slow and deep. The total ventilation per minute is less than for normal females, 6.62 litres per minute as against 7.98. In sleep the depth is greatly diminished being rather smaller than that of schizophrenics (317 as against 339 c.c.); the rate becomes slightly faster than in the dozing state, and the total effective ventilation is about half of that of normal subjects.

DISCUSSION.

THE SIGNIFICANCE OF THE RAPID SHALLOW TYPE OF RESPIRATION.

The question arises whether rapid shallow breathing is as effectual a method of ventilating the lungs as deep slow breathing. At first sight the fact that the total volume breathed per minute in each case is about the same, might seem to show that each is equally effective, but certain considerations are against this view.

In considering this matter, account must be taken of the so-called dead space, or space within the respiratory passages which prevents a certain proportion of tidal air from reaching the alveoli. It is still a matter for controversy among physiologists as to how much the dead space varies in size under different conditions of breathing. It is probable that it varies little, and if this is so, then increase or decrease of the depth of respiration is much more important than increase or decrease of rate, in altering the effective ventilation of the lungs.

The following figures from Roaf's "Physiology"[x] show how, if the depth of respiration in one subject

TABLE VII.

Volume of Respiration	Dead Space	Effective ventilation (obtained by subtracting the second from the first)
300 c.c.	172 c.c.	128 c.c.
400 c.c.	172 c.c.	228 c.c.
500 c.c.	172 c.c.	328 c.c.
700 c.c.	172 c.c.	528 c.c.
900 c.c.	172 c.c.	728 c.c.
1,200 c.c.	172 c.c.	1,028 c.c.
4 times		8 times.

is four times that of another, the effective ventilation of the former is eight times, not only four times, that of the latter, given that the dead space and rate of respiration are the same in both cases.

x A.E. Roaf. Textbook of Physiology 1924 p. 237.

If, however, the rate of respiration is four times as fast in one subject as in another, where the depth is the same, then the effective ventilation is only four times as great.

Supposing, therefore, as is not unlikely, that the dead-space of the schizophrenic patients is of the same magnitude as that of normals, then the fact that they breathe more shallowly will not be compensated for by the greater rate of respiration.

The work of Haldane, Meakins & Priestley, 1919 (11), indicated for the first time how dangerous this type of respiration might be. They showed that in the absence of opposing factors it might be productive of definite signs of oxygen want. That this want may be demonstrated in terms of arterial desaturation, was shown by Meakins & Davies 1920. (20).

TABLE VIII.

From Meakins & Davies, p. 99.

Respiration			Oxygen per cent. arterial satura-tion.	Expired air.		Bar. m.m. merc.
Rate per. min.	Vol. per minute	Vol. per Respira-tion.		CO_2 per cent by volume	O_2 per cent by volume	
17.5	10.3 L	586 c.c.	94.3	3.49	17.09	763
35.0	13.5 L	385 "	93.6	2.87	17.6	763
48.0	15.9 L	315 "	91.7	2.49	18.6	757

The manner in which this type of respiration could produce oxygen want has been studied by Haldane and his co-workers. Keith (17) has shown that the manner in which the lungs expand (that is, like a Japanese fan) makes it necessary for efficient breathing to be deep rather than rapid.

He has also pointed out that expansion of the lungs does not take place constantly and uniformly throughout, and that the rapid shallow type of breathing would of necessity exaggerate the uneven distribution of air.

It may be remarked that the percentage of the oxygen in the alveolar air provides no indication of the degree of oxygen saturation in the arterial blood. Meakins & Davies (20) discussing the rapid shallow type of breathing reach the following conclusion: "Thus the average composition of the

> alveolar air may remain constant as regards percentage of oxygen, as is usually the case; or when the breathing is abnormally shallow, the oxygen content of the average alveolar air may rise above the normal level even though at the same time the arterial blood is inadequately supplied with oxygen."

Shallow rapid breathing, however, is not <u>necessarily</u> accompanied by low oxygen saturation of the blood. Binger, Brow and Branch, (2), found shallow rapid breathing could be produced in animals by injections of starch into the femoral vein. Yet as a rule there was no anoxaemia, although the latter, when present, did increase the rate still further.

Whether the arterial blood in schizophrenia is saturated with oxygen to an abnormally low degree could only be ascertained by direct experiment.

A report on this subject has been made by L. Segal and L.E. Hinsie[x], on the basis of an examination of 14 cases of cyanosed schizophrenics. They found that there was an abnormal degree of oxygen desaturation in 9 out of 14 cases. Whereas the normal low limits of percentage desaturation are between 100 and 94.4 per cent, 12 out of the 14 showed arterial blood which was less than 95 per cent. saturated with oxygen, and 6 were below 90 per cent. In the same series the oxygen content of venous blood was also found to be low. The oxygen consumption was high. The carbon dioxide content of arterial blood and the carbon dioxide content of the venous blood agreed with the normal

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findings. The authors concluded that the cyanosis in these cases resulted from incomplete oxidation of the blood in the lungs and secondly increased reduction of oxy haemoglobin to reduced haemoglobin in the peripheral capillaries.

To sum up our findings so far, the present investigation has elicited the important fact that schizophrenics breathe in a way described by Haldane as inefficient and even dangerous. This type of breathing may in the ways described above lead to oxygen desaturation of the arterial blood. Whether this is actually so or not remains to be studied further. One report cited above concludes that such is in fact the case.

With regard to patients in a more severe catatonic state, Gullotta has remarked that catatonics breathe more slowly than other schizophrenics. Mignot and Le Grand (op. cit.) stated that 18 catatonics examined by them breathed more slowly than normal subjects. De Jong and Baruk describing catatonia, talk of a "respiration très faible, presque suspendue en apparence". In the present investigation at Colney Hatch, it was very difficult to find any patient in a really severe catatonic state. The modern system of occupational therapy has made the "stuporous catatonic" a rare sight for the visitor. The most stuporous catatonic in my series had a tidal air of 491 c.c. and a rate of 13 per minute. This gave the total respiration per minute as 6.38 litres. (cf. Table IV. where the figure for the average male normal is 9.59 litres and for the average male schizophrenic 8.67 litres). Observations in the present series supported Gullotta's conclusion that in severe catatonia the breathing is slower than in other schizophrenics. It may be, therefore, that the shallow breathing of schizophrenics is to some extent compensated for by increased rate, but that when the rate falls during an increase in the catatonic state, then the oxygen desaturation of arterial blood proceeds further, this being represented clinically by cyanosed extremities and torpor of mind. Clinical experience at least goes to show that where respiration is improved by enforced exercise (G.F. Peters, (25)) or occupational therapy, as is the rule in most mental hospitals, the mental condition also improves.

<u>Comparison of Type of Respiration with that found in</u>

Sleep.

One rather paradoxical fact has emerged, namely, that the type of respiration in moderate degrees of catatonia is the exact opposite of that found in individuals who are in the drowsy state between sleeping and waking. A German writer, Grotjahn (9), has made a thorough study of the resemblance of this mental state to that found in schizophrenia. Yet the breathing in the drowsy state is deep and slow (Table IV.). It is when the drowsiness is replaced by sleep that the respiration takes on the same shallow character as in schizophrenics. In sleep, however, it remains slower than any but the most severe cases of catatonia.

Bearing of type of Respiration on Susceptibility of Tuberculosis.

The type of respiration is of interest in another connection. As is well known, tuberculosis is particularly common among these patients. Kahlbaum (15) in his great monograph on Catatonia wrote -

> "Es darf angenommen werden dass die Katatonie und die durch diese Krankheitsform gesetzten Lebensverhältnisse eine gewisse Disposition zu dem Tuberkel-Processe mit sich bringen.

Von anderen somatischen Krankheitsformen ist eine besondere Beziehung zur Katatonie von mir nicht bemerkt worden."

T.S. Clouston (1863) (4) wrote that "Tubercular deposition is about twice as frequent in the bodies of those dying insane as in the sane .. .... A majority of the cases of general paralysis and mania die non-tubercular, a majority of the cases of melancholia, monomania and dementia exhibit proofs of tuberculosis after death."

The greater liability to tuberculosis on the part of schizophrenics has often been attributed to their poor physique generally. The present study, however, suggests that the shallow character of their respiration might render the lungs more liable to the disease owing to their insufficient expansion.

SECTION III.

THE RESPIRATORY RHYTHM IN NORMAL AND PSYCHOTIC SUBJECTS.

SECTION III.

THE RESPIRATORY RHYTHM IN NORMAL AND PSYCHOTIC SUBJECTS.

In the previous section it was found that schizophrenic patients breathed on the average more shallowly and more rapidly than normal subjects. In the present section an attempt is made to examine the respiratory rhythm in normal subjects and then to compare it to that found in individuals suffering from schizophrenia, the manic depressive psychosis and epilepsy.

The apparatus used to take the records of these patients was that described above. When this instrument is used, the subject need have nothing strapped round his chest or abdomen. He is unaware that his respiration is being examined, and therefore the possibility of conscious interference with rhythm is eliminated.

In this section a totally different type of investigation is proposed. The respiratory movements as well as being concerned with oxygen and carbon dioxide exchange have, in the phylogenetic development of man, become closely associated with the higher centres of the brain, more especially those connected with speech.

It has long been known that changes in thought are accompanied by changes in respiration.

This subject has been studied by various workers since the time of Mosso, and it is worth while recapitulating the conclusions arrived at by succeeding observers.

SUMMARY OF PREVIOUS LITERATURE ON THE RHYTHM OF RESPIRATION.

Towards the beginning of this century considerable interest was taken in the character of the respiratory curve. The chief object in view was to ascertain whether certain states of mind were accompanied by characteristic types of respiratory record.

Several contributors to Wundt's "Philosophische Studien" and later "Psychologische Studien" discussed this problem.

An article by Rehwoldt (28) for instance illustrates the thoroughness of some of these investigators. He applied six bands round the subject's thorax and abdomen. Attempts were

TABLE IX.

showing alleged effects of Mental States on Respiration.

Author	Pleasant Sensation	Unpleasant Sensation	Sudden Emotional Reaction	Voluntary Attention	Revery
Mosso				Slow	Fast, Deep and Irregular
Rehwoldt			Fast and deep		
Lehmann	Deep and Regular	Deep Irregular			
Mentz	Slow	Fast			
Zoneff and Meumann	Shallow and fast	Deep and Slow		Fast & shallow (but great individual differences)	
Angell and Thomson	Little affected	Little affected	Irregular	Regular generally Irregular when tendency to vocalise	

made to ascertain if there were characteristic curves in such conditions as hilariousness, aesthetic pleasure, bliss, or enthusiasm. Also in anger, depression, rage, pain and tension. The results of these investigations were for the most part negative. He concluded that affects could be divided into three classes

(1) Restful affects.

(2) Affects with excitement.

(3) Tension.

Diminution in the height of the curve occurred in (1) and (3), increase in (2). The rate of respiration was greater in (2) than in the other two conditions.

Lehmann (18) was especially interested in the effect of pleasant and unpleasant impressions. He believed that the former increased the depth of respiration, and that strong unpleasant impressions were accompanied by several deep respiratory movements. Mentz (21) concluded that pleasant feelings caused a slowing of respiration while unpleasant quickened it.

Zoneff and Meumann (33) made a very exhaustive study in normal individuals employing various stimuli, optic, acoustic, gustatory, cutaneous and psychic (arithmetical problems and space conceptions) and studied at the same time the effects of voluntary attention and pleasant and unpleasant impressions on the respiration.

They found that there were great individual differences but that voluntary attention usually caused increase in rate but decrease in depth, sometimes amounting to inhibition of respiration. They believed that pleasant sensations caused shallowing and acceleration, but unpleasant sensations deepening and slowing. Reference to the accompanying table will show how conflicting the results arrived at by these investigators were.

In England, Angell & Thomson (1899)[1] made a contribution to the subject. They refer to the work of the physiologist Mosso who had previously given much of his attention to this subject. He studied chiefly the effects of emotion and found that it was "impossible to make any satisfactory classification of breathing types as connected with mental activity or emotion.

Angell & Thomson themselves came to very reasonable conclusions. They found that the respiration tended to be regular where the organism was undisturbed by changes in the environment, that is, so long as the subject's equilibrium was maintained. In voluntary attention the rhythm was generally regular. They mentioned incidentally that where there was a "tendency to pronounce words" as when the subject was asked to remember nonsense syllables, the breathing became irregular.

An important contribution to the subject was made by F. Peterson and C.G. Jung (26) writing in "Brain" in 1908. They studied the pneumographic curve in conjunction with the so-called psychogalvanometer. Among other things they studied the characteristics of the normal curve, and the effect on it of emotional stimuli and also of attention. They also studied the same phenomena in schizophrenics. Their material however was small compared with that studied in the present investigation.

In this article they made some observations which are of interest in relation to the present investigation.

> "It is altogether probable that there are more inexplicable influences at work in relation to the pneumographic curve than we are at present

able to comprehend. There are many respiratory fluctuations which have nothing to do with the emotions, but are the result of physical or intellectual processes, together with the enforced quiet of the body at rest, the test person, with the disposition to speak, etc."

"Again, when the emotions are very labile, and show the most marked excursions in the galvanometer curve, the respiratory curve is often regular and even. On the other hand in instances both normal and pathological, where the galvanometer curve is marked by little fluctuation, or even by none, as in some cases of catatonia, there will often be most decided variations in the pneumographic curve. There does not seem to be the intimate and deep relationship between the respiratory function and unconscious emotions that exist between the sweat glandular system (which influences the psychogalvanometer) and the emotions ..... Respiration is an instrument of consciousness. You can control it voluntarily while you cannot control the galvanometer curve. The respiratory innervation is closely associated with speech innervation, anatomically and functionally, and the physical connection in the brain is, perhaps, one of the closest and earliest." loc. cit. pp. 173 - 175.

One of the most important advances in the above paper was the observation that there are irregularities in the respiratory curve which have not to do primarily with emotion. Also that there is a close connection between the intellectual faculty especially the faculty of speech and the respiratory function.

These facts were further elucidated by Golla and Antonovitch 1931, (7) also writing in "Brain".

These observers examined 67 normal subjects with reference to the regularity of respiratory rhythm. Neglecting the emotional factor, which they believed to be easily recognisable when it occurred, they directed their attention to a subjective examination of the mental content of these individuals. They were at once struck by a correlation between visual imagery and regular breathing on the one hand, and auditory imagery and irregular breathing (with a tendency to vocalise) on the other.

Of the 67, 34 were classed as regular breathers. All except one had considered themselves to use predominantly visual imagery. The remaining one had said he used predominantly auditory imagery. Thirty-two subjects showed an irregular rhythm and of these 28 had been assessed by their answers as using predominantly auditory imagery, the remaining four being classed as visualists. One had been doubtful.

In discussing the significance of the two types of respiratory rhythm, these writers point out that in their experiments irregular rhythm frequently became regular when a problem was set, the solution of which required purely visual imagery. They considered that irregular respiration was caused by the use of a kind of internal speech. They added, however, that it would be wrong to assume that such irregularity of rhythm is in any sense a point-to-point representation of the actual respiratory disturbance that would take place if the auditory images were to be translated into spoken words.

If this were so, such images could only occur, as in speech, during the expiratory phase, whereas any one belonging to the auditory type is conscious that the images arise uninterruptedly both during expiration and inspiration. The irregularity is of a less definite character, the diaphragm and thoracic, as well as the laryngeal, muscles helping to cause it.

SCOPE OF THE PRESENT ENQUIRY.

The object of the present enquiry has been to find out with the improved apparatus if there was any particular mental process which in normal subjects gives rise to a special type of respiratory tracing. The results of the investigations just quoted for instance would seem to indicate that auditory imagery with a tendency to vocalisation gives rise to an irregular type of respiration.

Secondly, was there any feature which was more frequently found, or solely found, in the respiratory tracing of a psychotic as compared to a normal individual?

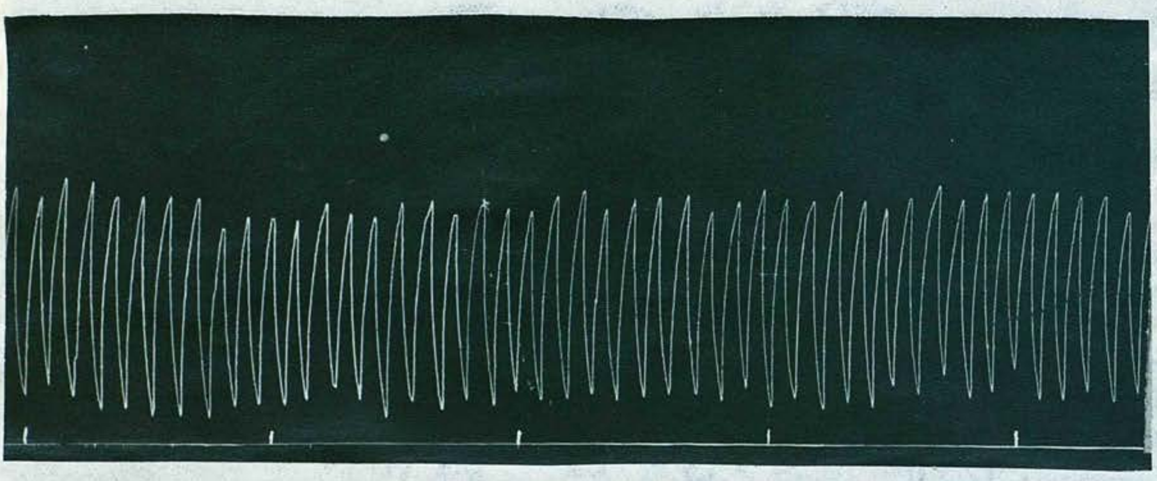
Thirdly, were the respiratory reactions of psychotic subjects to various stimuli different from those of normal subjects? In what follows an account is given of the results obtained, and also a discussion of how far the questions stated above are answered.

Respiratory Rhythm in Normal Subjects. In the present series 65 normal subjects were tested. These were nearly all members of the staffs of the Maudsley and Colney Hatch Mental Hospitals, who kindly consented to co-operate in this work. The first problem to be examined in each of these experiments was whether the individuals showed either predominantly regular or irregular rhythm (Figs. 3 and 4.)

Of the 65 normal subjects, 45 males and 20 females, 32 (22 men and 10 women) were regular breathers, while 33 (23 men and 10 women) were irregular. These figures corresponded roughly to the figures of Golla and Antonovitch quoted above, who found that of 67 normal cases, 54.5 per cent. were regular and 45.5 per cent. irregular.

An attempt was made to eliminate from the outset any physical causes of irregularity. Any

Fig. 3.



Example of Regular Breathing. Time signal 30 seconds.

(In all these figures upstroke represents inspiration.)

See page 64.

tongue or lip movements in the nature of a tic caused irregularity. It was possible, however, for the observer to stand at the side of the subject and watch for any movement of the lips or tongue. If any such were seen, the record was discarded. Another factor which influenced the rhythm was catarrh of the respiratory passages. All the subjects were free from this at the time of examination. Any marked restlessness on the part of the individual was apt to cause a characteristic kind of irregularity, although small movements failed to interfere with the predominant rhythm.

As might be expected, the respiratory curves were also affected by any emotion of even moderate degree. The whole subject of the effect of emotion on respiration is a wide one, as has been indicated, and it is not proposed to discuss it here. The nature of the change caused by emotion, whether to deeper or shallower breathing, depends on a variety of causes, which have been studied by the workers quoted above. In what follows, it is only pointed out that the irregularity caused by emotion is of a different type from that under discussion.

Where the respiration was influenced by emotion, it would suddenly change and then return to normal after a number of breaths. For a record where the phenomenon was frequent, the term "labile" seemed applicable. The true irregularity of rhythm which is the present subject for study is something different. The irregularity is rather from one respiration to the next, not from series to series. (Fig. 4). The change of respiration to deeper or shallower for a while following emotion might characterise either a regular or irregular record.

It was impossible to tell beforehand which individual would be regular and which irregular, merely by noticing the degree of "nervousness". Some cases of anxiety neurosis were very regular, and also not labile, while some apparently apathetic subjects were irregular.

Neglecting therefore the question of emotion, the writer proceeded to test the degree of auditory imagery with its tendency to vocalise, in these subjects. He asked a number of individuals to think out a problem while sitting in the apparatus. They did not know during the test that their respiration was being tested. The inquisitive were merely told that the apparatus had in some way to do with metabolism. The first problem was of such a kind that the subject would most easily solve it by using not auditory, but visual imagery. He was asked first to look at a sheet of paper which showed each of the capital letters of the alphabet. He was then asked to picture each letter as he would see it in a mirror. He was told that at the end of the experiment he would be asked which of the letters looked the same in the mirror as when looked at direct. This ensured that the subject would concentrate as thoroughly as possible.

In fact, A H I M T U V W X Y appear the same in a mirror as when looked at direct. If an individual for instance included N S and Z he was considered to have a bad capacity for visual imagery. This was called the visual test.

Secondly the subject was asked to perform a task for which most people would use auditory imagery. It had been found from previous questions that most people used predominantly this type of imagery in adding up a column of figures. This test was set, and may be referred to as "the auditory test".

In all, 44 normal individuals were examined. Eighteen or 41.0 per cent. were regular in one test and irregular in the other. Of these 18 all except one exhibited the regular rhythm in the test for which visual imagery was indicated, but irregular rhythm in the test for which auditory imagery was commonly used. One of these is shown in Fig. 5. In only one doubtful case was the rhythm regular in the adding test and irregular in the visual test.

Of the 44, 13 or 29.5 per cent. were regular in both tests and the same number were irregular in both tests.

Subjective tests (which will be described later) indicated that 12 of those 13 regular breathers employed predominantly visual imagery, while 10 of those 13 irregular breathers had a preference for auditory imagery.

From the fact, then, that 17 out of 18 individuals showed regular rhythm during the test where visual imagery was indicated, but irregular

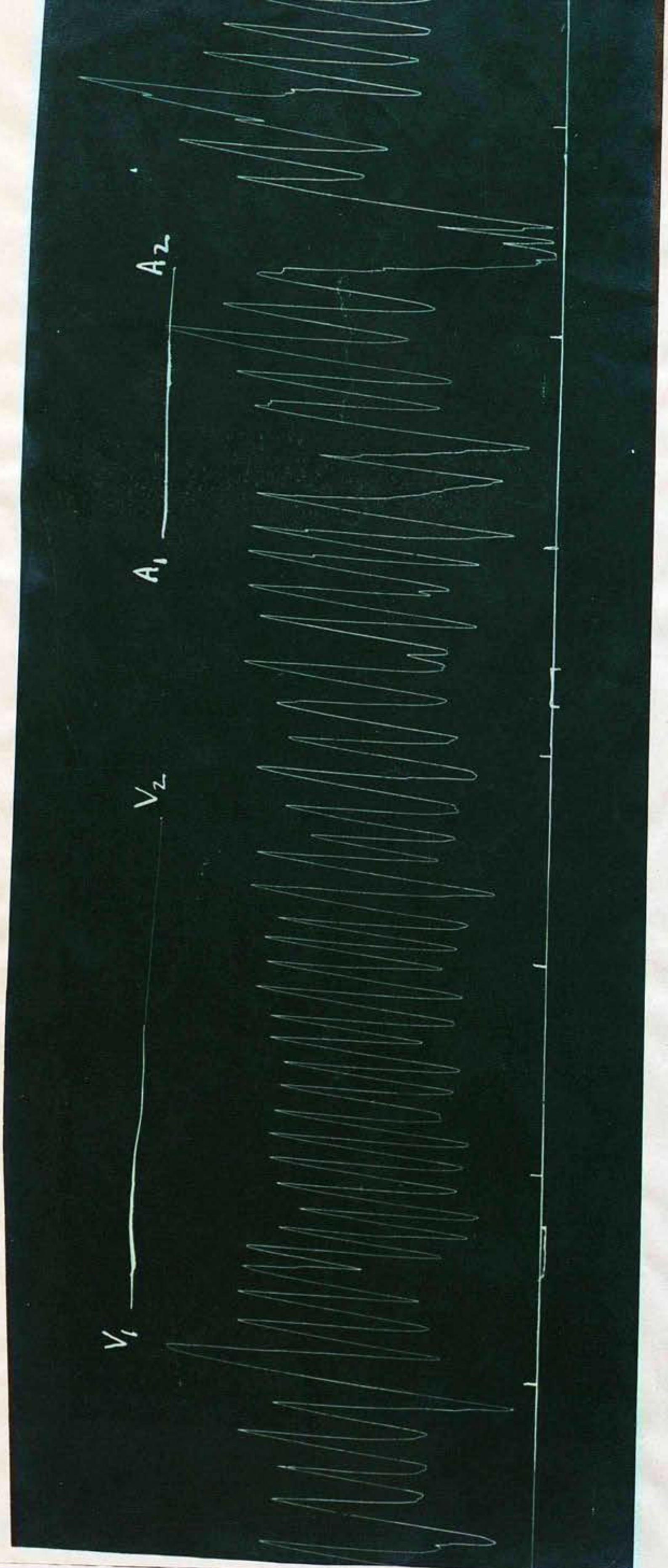


FIG. 5.

This subject shows regular breathing during "visual test" ($V_1 - V_2$) and irregular breathing during "auditory test" ($A_1 - A_2$).

Time signal 30 seconds.

See page 68.

rhythm where auditory imagery was more suitable, it may be deduced that respiration tends to become regular where an individual is employing visual imagery, and irregular when using auditory imagery.

The fact that 13 individuals breathed regularly both during a test for which visual imagery was indicated and also during a test where visual imagery might or might not be used, suggested that these individuals preferred to employ visual rather than auditory imagery wherever possible. The fact that 13 subjects used irregular rhythm throughout seemed to indicate that they were individuals who had difficulty in using visual imagery exclusively at any one time, even where the problem seemed to require the visual type of thinking.

As already stated it was confirmed by subjective tests that 12 of the 13 subjects who breathed regularly throughout both tests employed predominantly visual imagery, while 10 of the 13 whose rhythm was irregular throughout, used predominantly auditory imagery.

It has already been stated that tests were carried out on these normals to find out which type of imagery they used. These tests were partly subjective and partly objective.

The subject was first of all asked to think of a clock face with the hands pointing to twenty minutes past eleven. He was then asked to imagine that the big hand was the small hand, and the small hand the big hand, and further asked what the time would then be. The interval which elapsed between putting the question and receiving the answer was noted. The subject was then asked how he did the problem and how easily he could picture the clock face.

He was then shown a sheet of cardboard with the capital letters of the alphabet clearly printed on it. He had to picture each of the letters as he would see it upside down, and told that he would be questioned at the end of the test as to which letters looked the same upside-down as the right way up. In fact, H I N O S X and Z look the same upside down as the right way up. If an individual for instance included N.S. and Z he was considered to have a good visual capacity.

Lastly he was asked to look at these patterns  and to write them down from memory. The strongest visualists were those who wrote them straight down without saying the numbers to themselves. The strong auditories were those who translated the patterns into the sounds of the numbers and then translated them back again.

From these data it was recorded whether the subject used predominantly auditory or predominantly visual imagery. After he had been classed as auditory or visual the respiratory record was taken and examined to see whether the respiration was regular or irregular in type. (Table IX).

Of the 32 regular breathers, 24 or 75 per cent were visualists, while of the 33 irregular breathers 24 or 72.8 per cent were auditories. It would appear then from these figures that regular and irregular breathing are accompanied in a significant number of cases by visual and auditory imagery respectively.

Relation of Respiratory Rhythm to Visual and Auditory Imagery in the Hypnoidal State.

Still further experiments were devised to find out more conclusively whether a particular individual preferred to use auditory or visual imagery

TABLE IX. See page 71.

Relation of Regular or Irregular Rhythm to Type of Imagery (Visual or Auditory).

	Regular	Irregular	Visual	Auditory	Regular & Visual	Percentage of Regular Breathers who are visualists	Irregular and Auditory.	Percentage of Irregular Breathers who are auditories.
MEN	22	23	23	22	16	72.8	16	69.6
WOMEN	10	10	10	10	8	80	8	80
BOTH	32	33	33	32	24	75	24	72.8

in general. It was found that persons in a hypnoidal state have clearer mental images than in the waking state and further that they can generally remember them on waking up, if the hypnotic state has not been too deep. Accordingly seventeen individuals were successfully hypnotised while sitting in the apparatus. When in the hypnotic state it was suggested that they were in a school room where they were to do multiplication tables. They had the choice of hearing boys recite them or else seeing the multiplication tables on the wall. Of the seventeen subjects who were able to be hypnotised, eight when questioned after waking up, stated that they had seen the multiplication tables in the dream, five said they had heard the boys recite them while four said they both saw and heard the tables.

These same individuals while in the hypnotic state were also induced by means of suggestion to experience first visual and later auditory imagery. A silent country scene was suggested to them. Later it was suggested to them that they were listening to an invisible orchestra playing a tune.

TABLE X.

Class	Subject's Number	Usual Rhythm when Awake	Rhythm during visual dream	Rhythm during Auditory dream
Those who saw the multiplication tables	14	Reg.	Reg.	Irreg.
	13	Reg.	Reg.	Reg.
	2	Reg.	Reg.	Reg.
	7	Reg.	Reg.	Reg.
	10	Reg.	Reg.	Reg.
	12	Reg.	Reg.	Reg.
	4	Reg.	Reg.	Irreg.
	9	Reg.	Reg.	Irreg.
Those who heard the multiplication tables	1	Irreg.	Reg.	Irreg.
	5	Irreg.	Irreg.	Irreg.
	15	Irreg.	Irreg.	Irreg.
	6	Irreg.	Reg.	Irreg.
	17	Reg.	Reg.	Irreg.
Those who both saw and heard the multiplication tables	8	Irreg.	Irreg.	Irreg.
	11	Reg.	Reg.	Irreg.
	16	Reg.	Reg.	Irreg.
	3	Reg.	Reg.	Reg.

From the accompanying table it will be seen that

8 saw the multiplication tables (Class 1)

5 heard a voice recite them (Class 2)

4 saw and heard simultaneously (Class 3)

The rhythm was examined of such subjects, (a) when awake, (b) when dreaming a visual dream, (c) when dreaming that they were listening to a tune.

Class (1) were all regular during the visual dream, and also when awake. Three of these were irregular during an auditory dream.

Class (2) were all irregular during the auditory dream. Four out of the five were irregular when awake, and two were irregular during the visual dream.

Class (3). Three of this class were irregular during the auditory dream, and three were regular during the visual dream. Three were regular when awake.

None of those who were regular throughout used auditory imagery from choice, and none of those who were irregular throughout used visual imagery from choice.

By these results the former conclusions are strengthened, namely that those who have a preference for visual imagery breathe regularly, while those with a preference for auditory imagery breathe irregularly.

These results were taken as showing that individuals vary considerably in their tendency to vocalise when thinking. Where this is present, the subject finds himself employing sound images, and his breathing is irregular. Where there is no tendency to vocalise, the respiration remains regular and the imagery is visual.

It may be mentioned that an attempt was made to discover which of the hypnotised subjects possessed what might be called a strong kinaesthetic imagery. It is in virtue of this faculty, for instance, that one individual stated that when he thought of letters upside down, he did not picture them, so much as imagine himself turning them round. One individual stated that he never had visual imagery in dreams, yet he often dreamt he was playing hockey, having only the sensations of movement in the dream. Another said that he dreamt he was driving a car, having the sensations of turning the driving wheel, manipulating the brakes, etc., without seeming to see or hear anything.

In the present investigation it was suggested to the subject for experiment while in the hypnotic state that he was starting to run up a hill. During this dream his respiration was recorded. Later when he awoke he was questioned as to the vividness of the sensations of movement.

No correlation was discovered, however, between vividness of kinaesthetic imagery and regularity or irregularity of respiration. Table XI.

TABLE XI.

Class	Subject's number	Usual Rhythm when Awake	Rhythm during visual imagery	Rhythm during auditory imagery
Those with doubtful kinaes-thetic imagery	1	Irreg.	Reg.	Irreg.
	5	Irreg.	Irreg.	Irreg.
	13	Reg.	Reg.	Reg.
Those with vivid kina-esthetic imagery	10	Reg.	Reg.	Reg.
	11	Reg.	Reg.	Irreg.
	12	Reg.	Reg.	Reg.
	8	Irreg.	Irreg.	Irreg.
	9	Reg.	Reg.	Irreg.
	5	Irreg.	Irreg.	Irreg.
	2	Reg.	Reg.	Reg.
	3	Reg.	Reg.	Reg.
	4	Reg.	Reg.	Irreg.
	16	Reg.	Reg.	Irreg.
Those with weak kina-esthetic imagery	7	Reg.	Reg.	Irreg.
	14	Reg.	Reg.	Irreg.
	15	Irreg.	Irreg.	Irreg.
	17	Reg.	Reg.	Irreg.

In these records no connection can be seen between regularity and the presence or absence of kinaesthetic imagery. Of those who stated they were conscious of movement, three were regular throughout and two irregular throughout. Of the four cases who had no kinaesthetic imagery three were regular and one irregular in the waking state.

These findings are in keeping with the work recorded above by previous writers. Peterson and Jung had concluded that regularity was dependent more on intellectual than on emotional factors. The above results would bear out the supposition that where there is no tendency to think in terms of one's own voice the rhythm is peculiarly regular. Where, however, the individual is inclined to vocalise, the rhythm becomes irregular. This irregularity would seem to be dependent on movements of muscles of the chest to a greater extent than of those of the larynx, being noticeable on the record during inspiration, as well as expiration. Those who do not tend to think in terms of their own voice, or use a kind of inner speech, appear from the above results to use predominantly visual imagery.

Further work remains to be done to elucidate the relation of type of rhythm to type of imagery. For instance the respiration of a series of congenitally blind individuals might be tested in order to ascertain whether they breathed irregularly, and a series of congenitally deaf individuals in order to see whether their respiration were regular. (The latter test would not be so conclusive, since nowadays such patients are taught to vocalise from an early age.)

Respiratory Rhythm during Normal Sleep.

Eight records of three different subjects who fell asleep in a plethysmographic apparatus made on the same principle as that used in the present series was compared to the above records. I am indebted to Dr. Antonovitch for these records, hitherto unpublished. In each case the subject became more irregular in the dozing state which preceded sleep. During sleep the subject became regular. In the case of one who was fairly regular when awake, the rhythm became regular in sleep.

RESPIRATION IN PSYCHOTICS.

Records of 179 psychotic patients were examined. Of these, 133 were schizophrenic;

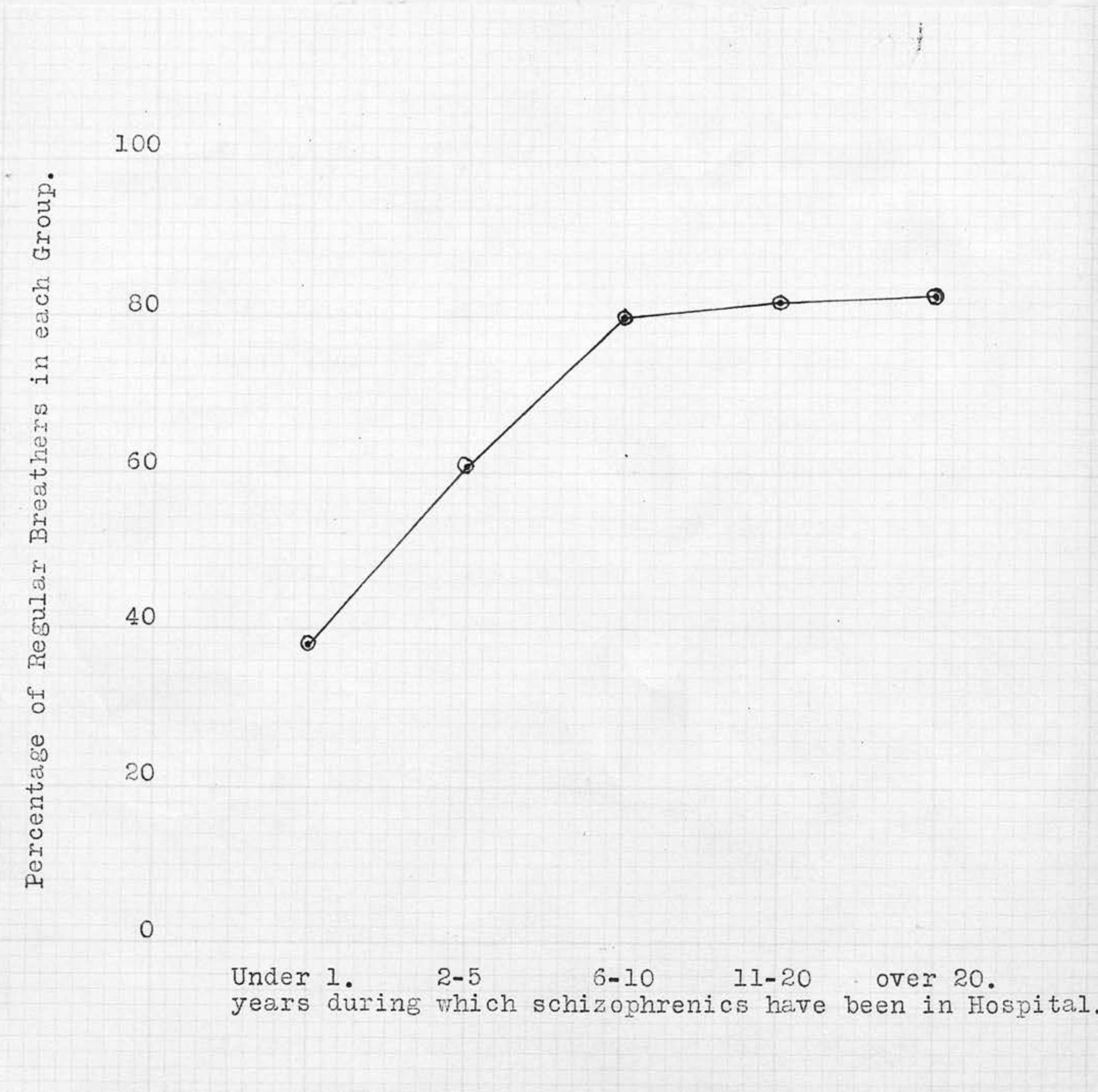
TABLE XII.

Relation of Regular or Irregular Rhythm to Duration of Mental Disease.

Length of time in Hospital.	Under 1 year		2-5 years		6-10 years		11-20 years		Over 20 years		Total
	Reg.	Irreg.	Reg.	Irreg.	Reg.	Irreg.	Reg.	Irreg.	Reg.	Irreg.	
SCHIZOPHRENIA											
Males	7	16	12	6	13	3	22	4	15	2	100
Females	4	2	2	3	3	1	1	1	15	4	36
Total	11	18	14	9	16	4	23	5	30	6	136
MELANCHOLICS											
Males	7	5	0	1	0	0	0	0	0	0	13
Females	7	4	0	5	0	0	0	3	0	0	19
	14	9	0	6	0	0	0	3	0	0	32
EPILEPSY											
Males	0	1	2	1	0	1	0	0	8	1	14

FIG. 6

Percentage of Regular Breathers among schizophrenics in relation to time in Hospital.



The percentage of Regular Breathers rises from 38 per cent. in those admitted less than a year previously to 83 per cent. of those who have been in Hospital more than 20 years.

32 were melancholic, and 14 were epileptic. As has been already reported, the schizophrenics differed on the average from normal subjects in that their breathing was shallower and more rapid.

The rhythm of respiration in schizophrenic patients was studied to find out whether it differed in respect of regularity or irregularity from that of normal subjects. The same technique was employed as previously in the case of normal subjects. In all, 136 schizophrenics were examined, 100 males and 36 females. Of these, 94 were classed as regular and 42 as irregular. This represents 69.1 per cent. of regular breathers as compared to 49.2 per cent. of regular breathers in the normal group. Examination of the schizophrenic group showed that the irregular breathers were mostly to be found among those who had been ill for less than five years. (Table XII. and Fig. 6). It will be seen from the Table that out of those who had been in hospital for less than one year 11 were regular and 18 irregular. Fig. 6 shows how the percentage of regular breathers goes up according to the length of time that the patient has been in hospital.

Further analysis of the figures, however, showed that the difference between the percentage of regular breathers among the schizophrenics who had been in hospital less than one year, and those who had been in from two to five years was not significantly different. Neither of these groups was significantly different from normals. All the schizophrenic groups, however, who had been in hospital more than five years showed a significantly greater percentage of regular breathers than the other three groups, namely, (1) the normal group; (2) the group of patients admitted less than one year and (3) the group of patients admitted 2 - 5 years previously.

When we examine the records of 32 melancholic patients we find that 14 are regular and 18 irregular. (As only 3 of these had been in hospital more than five years, it was not possible to correlate regularity with the duration of the illness, as has been done in the case of the schizophrenics.)

Of the epileptics who had been in more than 20 years, eight were regular and one irregular. These were all considerably demented. Of those who had been in less than five years, 2 were regular and 2 irregular.

It may be observed, then, from these cases that where there is considerable dementia whether in schizophrenics or epileptics, the respiration is usually regular. The most regular were those who were not able to do work of any kind.

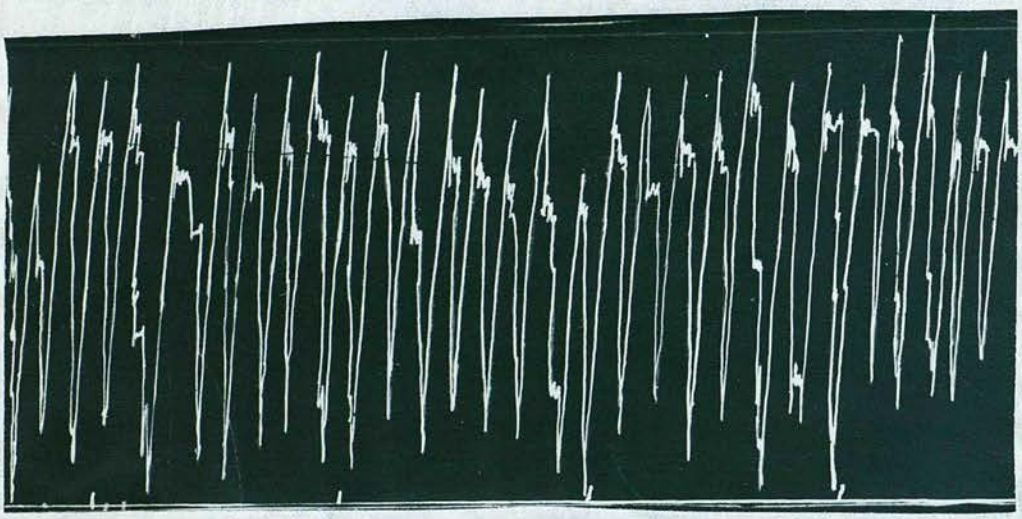
No marked difference could be seen between the record of the typically regular normal and that of the typically regular schizophrenic. The extremely regular type of rhythm however, such as is found in sleep, was commoner among schizophrenics than normals. There was no obvious difference between the typically irregular normal and the irregular schizophrenic.

Some schizophrenics, however, gave rather unusual respiratory records, such as periodic holding of the breath, (Fig. 7). Another showed a curious tremor of the respiratory muscles during each respiration (Fig. 8). There were still other unusual records which were in keeping with the rhythmical and bizarre character of other schizophrenic symptoms.

Records showing Hallucinations.

It not infrequently occurred in one of these

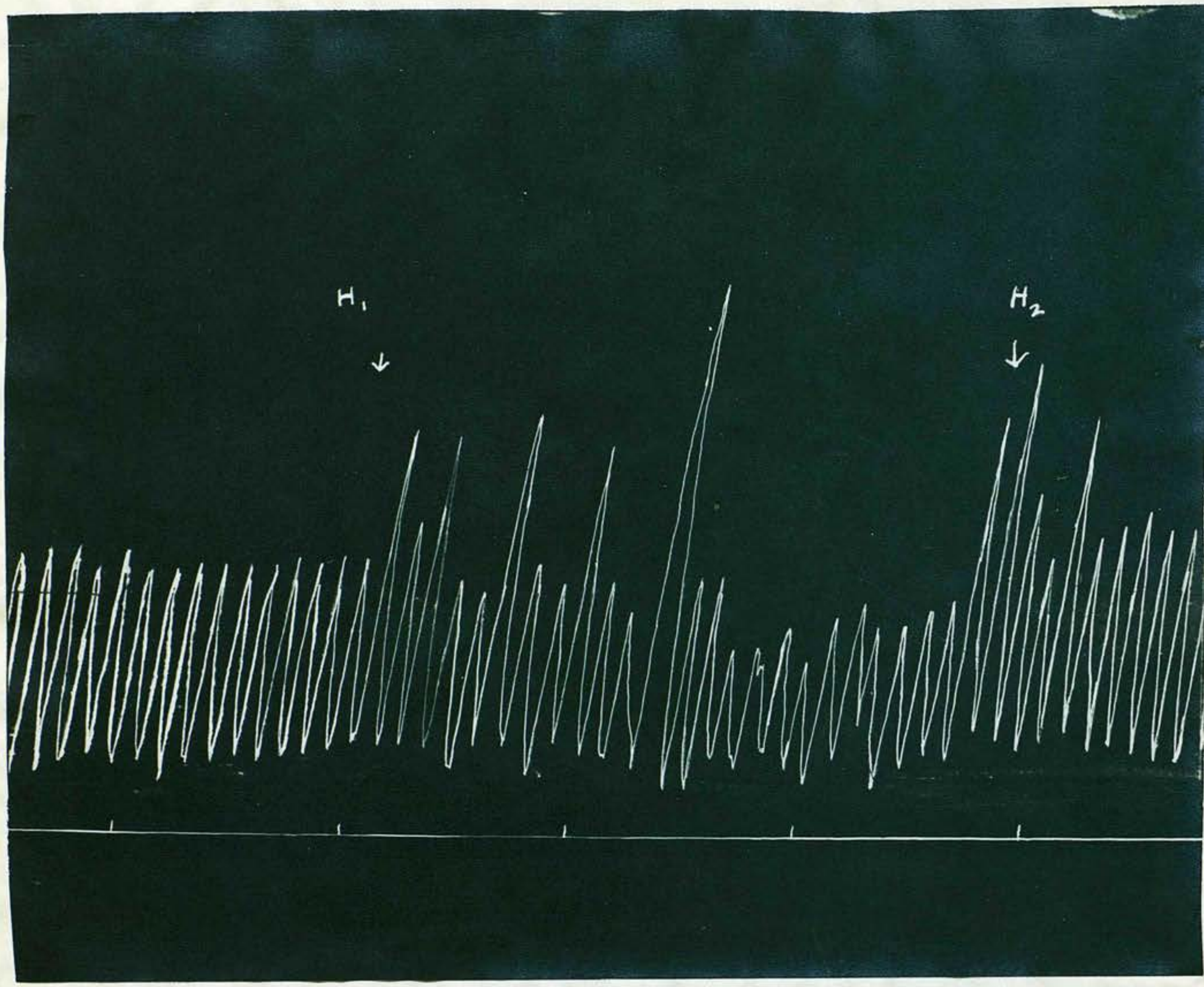
FIG. 8.



Rhythmical tic-like respiratory movements in a schizophrenic.

Page 82.

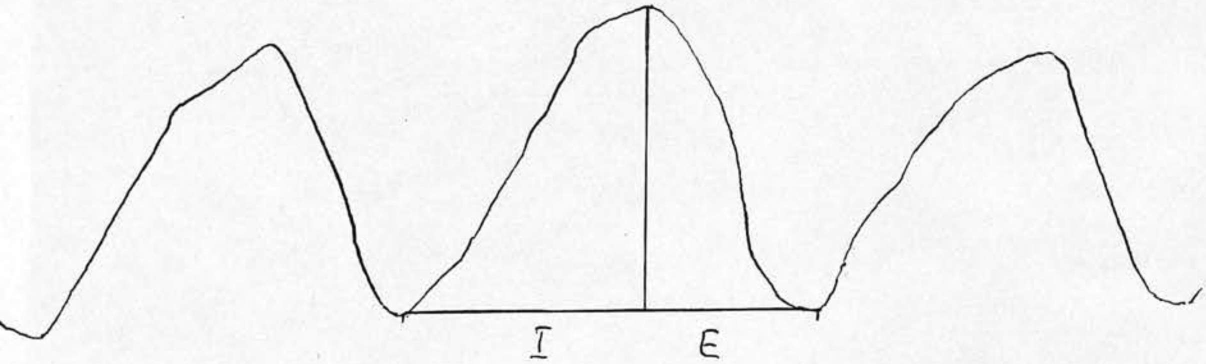
FIG. 9.



Schizophrenic, a regular breather, shows irregular respiration between H_1 - H_2 during which time he was hallucinating. No movement of lips or larynx were noticeable.

See page 83.

Fig. 10.



To show the I/E ratio described by some writers as being different in schizophrenics from normals. Inspiration is shown by an upstroke, and expiration by a downstroke. I shows the duration of inspiration, and E of expiration.

experiments that while a patient was breathing regularly he suddenly started to breathe irregularly. (Fig. 9). When questioned, he would say that he had heard a voice speaking to him, even although his lips had not been observed to move. On more than one occasion this occurred where the patient had denied hallucinations, but later admitted them, when asked about his thoughts at the moment when his breathing changed.

On other occasions sudden irregularity of breathing was found to be accompanied by olfactory hallucinations.

THE I : E RATIO.

Some writers have claimed to find a difference in the character of the respiratory curve obtained from schizophrenics as compared to that obtained from normals. In these experiments inspiration is represented on a moving drum by an upstroke and expiration by a downstroke. One can compare the duration of inspiration with that of expiration.* The duration of inspiration divided by the duration of expiration has been called "inspiration-expiration ratio". The

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* See Fig. 10.

expiration period lasts from the end of inspiration to the beginning of the next inspiration and so includes the respiratory pause.

Now, if the rate of respiration be decreased the decrease in rate occurs chiefly at the expense of the respiratory pause. Since, then, the respiratory pause is included in the expiratory phase, E will be relatively longer. For instance, Mignot and Le Grand studied a few cases in which there was especially slow respiration. They therefore found that the I : E ratio from being 10:14 in normals was as much as 10:20 or even 10:80. Since however in most cases of schizophrenia the rate of respiration is increased, the I : E ratio is less than 10:14.

Other Characteristics of the Respiratory Curve in Schizophrenics.

A great deal of the work done on this subject gave negative results. It has been said by an Italian Sandri (31) that in schizophrenics if inspiration is represented by an upstroke, the first-half is steeper than the second half. In normals it is said that this feature is much less marked. In expiration also, the first half of the downstroke in schizophrenics is said to be steeper than the second half. In the present series, however, no difference of such a kind could be seen in the plethysmographic tracings, nor in the thoracic nor abdominal tracings where these were also carried out.

REACTIONS TO STIMULI BY NORMALS AND SCHIZOPHRENICS.

Both normals and schizophrenics were subjected to certain disturbing factors, in order to ascertain whether the latter's change of respiratory depth and frequency was significantly different from that of the former. The first of these consisted of a mental exercise. Not only normals but also those schizophrenics who could give correct answers, were asked to add up a column of figures while sitting in the apparatus.

43 normals and 34 schizophrenics were subjected to this test. (Table XIII.) With the normals the height during addition was not found

TABLE XIII.

Comparison of undisturbed Respiration with that occurring during Mental Test (addition) and during Pinch, in Normals and Schizophrenics.

	Normals			Schizophrenics		
	h_1 47.5	f_1 17.9	v_1 824	h_1 38.7	f_1 20.3	v_1 786
Addition	h_2 49.6	f_2 22.1	v_2 1037	h_2 43.3	f_2 21.6	v_2 946
Difference	Not sig.	Sig.	Sig.	Not Sig.	Not Sig.	Borderline
	h_1 45.7	f_1 17.4	v_1 762	h_1 35.7	f_1 19.7	v_1 693
Pinch	h_2 37.2	f_2 18.3	v_2 654	h_2 29.6	f_2 18.4	v_2 521
Difference	Sig.	Not sig.	Not sig.	Sig.	Not sig.	Not sig.

h_1, h_2 = height of respiratory curve in m.m., during undisturbed state and during the respective tests. f_1, f_2 = frequency of respirations per minute.

v_1, v_2 = volume, product of h and f. "Sig" indicates that the difference between undisturbed and disturbed values is significant. In the "addition" test there were 43 normals and 34 schizophrenics. In the "pinch" test there were 20 normals and 20 schizophrenics.

TABLE XIV.

Effect of Stimuli on Schizophrenics compared to Normals. The differences were reckoned as percentages of the undisturbed value.

		Mean percentage of change.	Standard Error.
Volume of Respiration during addition	Volume for normals	+ 29.4	± 6.6
	" " schizophrenics	+ 17.7	± 5.8
Frequency of Respiration during addition	Frequency for normals	+ 30.0	± 7.2
	" " schizophrenics	+ 5.3	± 3.2
Height of Respiration during pinch	Height for normals	- 19.2	± 4.0
	" " schizophrenics	- 19.0	± 5.9

Only in frequency of respiration is the difference in normals significantly greater than in schizophrenics.

to be significantly different. This, however, may have been due to the fact that too few cases were examined. The frequency and also the total ventilation, however, were significantly greater during addition.

In the schizophrenic group the height and frequency were not significantly changed during the mental exercise compared to the undisturbed state. The change of total ventilation was found to be on the border line of significance.

20 normals and 20 schizophrenics were also subjected to a painful pinch. Following the pinch there was a significant decrease in the height of the curve both in normals and in schizophrenics. The changes in frequency and volume, however, were not significant in either class.

Statistical analysis showed that the only values of normals in both these tests which could be compared with those of schizophrenics were, (1) Volume of respiration in the addition test, (2) Frequency of respiration during the addition test, and (3) Height of respiration during the pinch. (Table XIV.)

It will be seen from the table that the only significant difference is in the frequency of respiration during addition. This is significantly greater in the normals than in the schizophrenics.

From the above figures, then, no very decisive conclusions can be drawn, owing to the relative amount of scatter, and the relative paucity of material. One can only say that the figures have not proved the existence of a greater or less reaction to pain in schizophrenics. They allow, however, of a tentative conclusion that there is a greater increase of the frequency of respiration during mental exercise in normals than in those schizophrenics capable of correct addition.

Both normal and schizophrenic individuals were also subjected to the sudden hoot of a motor horn and also to the light of a magnesium flare. The reactions, however, varied so much from individual to individual that no conclusion could be drawn.

DISCUSSION.

As has been already stated the whole subject of the relation of normal and pathological mental processes to the respiratory curve is a very large one.

In what follows an attempt is made to answer the three questions which were suggested in describing the scope of the present enquiry.

1. <u>Is there any particular mental process which gives a special type of respiratory record?</u>

In the present study there was seen to be a relation between the type of mental imagery, auditory or visual, and type of respiration, irregular or regular respectively.

As already mentioned, early investigators obtained no very clear results when they attempted to find characteristic respiratory curves for various emotions. Peterson and Jung (loc.cit), however, stated that the respiratory variations were associated with intellectual rather than emotional changes. Golla and Antonovitch (loc. cit.) went further and concluded that irregularity was associated with auditory imagery and regular with visual imagery.

In the present study the main argument to prove that regularity of rhythm tends to go with visual imagery was provided by the fact that where the subject was asked to work out a problem requiring visual imagery, the respiration was nearly always very regular except in those cases, where the individual appeared from subjective tests to find difficulty in using visual imagery at all. Again, subjects nearly always breathed with an irregular rhythm while doing a test which experience had shown usually to require auditory imagery, with a tendency to vocalisation, except where the individual found difficulty in employing any sort of auditory imagery.

An attempt was made to examine 65 normals by subjective and objective tests to see whether they used predominantly visual or auditory imagery. It was then found that regularity of rhythm corresponded to visual imagery in 75.0 per cent. of cases, and irregular rhythm to auditory imagery in 72.8 per cent. of cases. It is possible that these percentages might have been even higher if more appropriate tests had been carried out. These results were further supported by an examination of subjects in the hypnotic state.

A considerable amount of evidence, therefore, has been brought forward to indicate that regular breathing is accompanied as a rule by visual imagery and irregular by auditory imagery, the subject tending to use a kind of inner speech in the latter case.

2. Is there any feature which is more frequently, or solely, found in the respiratory curve of a psychotic compared to a normal individual?

It has been found that the respiration of schizophrenics is more shallow and more rapid on the average than normal subjects.

Further, those schizophrenics who had been in hospital more than five years showed a significantly greater percentage of regular breathers than either normals or recently admitted schizophrenics. About 83 per cent. of those who had been in hospital over 20 years were regular compared to 49 per cent. of normals.

Further work is therefore suggested on the subject of the mental imagery of schizophrenics, to find out whether these use predominantly visual imagery, and if so, whether it differs from that employed by most normal persons. The question as to whether the regularity of rhythm accompanies a mere cessation of mental processes, or a series of visual images remains undecided.

Schizophrenic patients were found on occasion to give peculiar kinds of records which would not be found in normal subjects. Some, for instance, showed a regularly recurring phenomenon such as holding the breath. Another feature which was characteristic of schizophrenia was extreme regularity of rhythm broken by a temporary extreme irregularity, followed again by a very regular rhythm. Yet during the irregular period the patient's lips or cheeks were not observed to move. These patients were found to be hallucinating.

3. Are the respiratory reactions of psychotic subjects to various stimuli different from those of normal subjects?

It was difficult to devise tests which would give sufficiently uniform results in normals to enable them to be compared to those obtained from schizophrenics. When those schizophrenics who were capable of giving correct totals in adding up a column of figures were compared to normals, the increase of respiratory rate was significantly less than the increase of rate during adding in normals. No conclusions could be drawn with regard to pain, sound or light reactions.

In conclusion I would state my indebtedness to Dr. C.P. Richter for allowing me to work in his laboratory at the Johns Hopkins Hospital, 1930-31. The work done then gave rise to Section I. of this thesis. A brief report of some of these experiments was given in the Arch. Neur. and Psych. XXIX. 1933 p. 231 ff. under the title "Action of Scopolamine and Carbon Dioxide on Catalepsy produced by Bulbocapnine" by A.S. Paterson and C.P. Richter. The conclusions however were somewhat different, being based on much fewer of my records. A brief report of

part of Section 2 also appeared in print in the Jour. Neur. and Psychopathology XIV. 1934 55 p. 323 entitled "The Depth and Rate of Respiration in Normal and Psychotic Subjects."

Dr. Percy Stocks, London, was kind enough to help me with the statistical work involved.

I would also acknowledge my indebtedness to Dr F. L. Golla for his constant interest and consultative help in the work recorded in Sections 2 and 3.

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S U M M A R Y.

SUMMARY.

Section I.

1. Preliminary remarks are made regarding the pathology of the serious forms of mental disorder grouped under the title of schizophrenia. Morbid anatomy and bacteriology which have been useful elsewhere have not found much scope here. Adolf Meyer's conception of the disorder as a progressive maladaptation of the individual to his environment does not negative the possibility of progress in our knowledge of the malady from the standpoint of psychology, heredity or physiology. As was the case with tuberculous patients, attention must be directed to the early stages of the disease, when physiological changes are first noticeable. In the present investigation, attention has been directed in the first instance to the physiological aspect of the disorder.

2. The system which has been chosen for study is the respiratory system. It has long been known that changes of respiration are closely related to cerebral function. Latterly Loevenhart, Lorenz and Waters reported that inhalation of high con-

centrations of carbon dioxide was responsible for a temporary relief from symptoms in cases of catatonic stupor. An account is given of the experiment described by these workers. The writer also carried out such an experiment at Baltimore.

3. Loevenhart, Lorenz and Waters were uncertain how far these phenomena could be explained at the physiological level, as the effect on muscle and brain of the carbon dioxide, or how far it was the manifestation of a psychological change. Others have thought that mere fright could explain the phenomenon.

4. The writer working with C.P. Richter was able to reproduce in macac monkeys, symptoms resembling those of catatonia by means of moderate doses of bulbocapnine. The animals were cataleptic, stuporous and showed certain autonomic nervous symptoms similar to those found in catatonics. He was able to test the intensity of the catalepsy by a special technique. This consisted of hanging the monkey at intervals from a bar. The length of time that the monkey remained suspended on each occasion corresponded to the intensity of the catalepsy. The

duration of the catalepsy was also measured, as the monkey refused to hang, when the effect of the drug wore off. Charts were thus made, the ordinates corresponding to the intensity, and the abscissae to the duration of the catalepsy.

5. In the present series, twenty-two records were made of the effect of carbon dioxide on the muscle tone of monkeys made cataleptic by bulbocapnine, as measured by the hanging response. The carbon dioxide was given in doses varying from 15 to 50 per cent, and was given as a rule when the catalepsy was submaximal. In general, doses of 15 per cent caused no increase of the cataleptic state, 25 per cent caused a marked increase, while 35 per cent and over, caused a temporary abolition of the catalepsy, followed by an augmentation or at least recurrence of the previous catalepsy. It was further observed that where the catalepsy was already maximal with bulbocapnine, as little as 15 per cent of carbon dioxide would cause the catalepsy temporarily to disappear.

6. Since moderate doses of carbon dioxide were found to increase the intensity of bulbocapnine

catalepsy, experiments were carried out to see whether carbon dioxide alone would produce the hanging response. Administration of 15 per cent failed to produce the response, or produced a slight transitory effect. Twenty five per cent produced it at once, when it might last for as long as 20 minutes. Doses of 35 per cent and over caused the reflex to disappear temporarily, after the administration ceased. The reflex returned within a minute, without further administration of the gas.

7. Using the word catalepsy in the narrow sense of "increase in muscle tone as measured by the hanging response", we can differentiate three states produced by carbon dioxide, namely the pre-cataleptic, the cataleptic and the ultra-cataleptic, resulting from small, moderate and high concentrations of the gas respectively. It thus resembles bulbocapnine, with which in this respect it is synergic, and not antagonistic to it. On the other hand, whereas the cerebral states with increasing doses of bulbocapnine are those of drowsiness, stupor and wild excitement, with carbon dioxide the animal is active in the first two phases, but, as a rule,

drowsy in the last. The monkey which has already been made cataleptic by bulbocapnine and then given carbon dioxide, assumes an appearance approaching normality. This is caused by the monkey passing into the ultra-cataleptic state, the cerebral condition resulting from the combined results of the two drugs, the one making for stimulation and the other for depression. The animal before becoming normal, has again to pass through the cataleptic phase.

8. Reference is made to the work of Giacomo who injected bulbocapnine into human catatonics. Some of these became more cataleptic, while others passed into a state of catatonic excitement. It is pointed out that these results are the same as are found when an additional dose of bulbocapnine is given to monkeys already made cataleptic by bulbocapnine. If the catalepsy is submaximal the animal becomes more cataleptic. If maximal, it passes into an ultra-cataleptic state resembling catatonic excitement.

9. The drug amytal which interrupts catatonic stupor was found to have an action on muscle similar

to that of carbon dioxide.

10. It is concluded from these experiments that the action of carbon dioxide on catatonic stupor in man is not strictly antagonistic. On the analogy of its action on monkeys made cataleptic by bulbocapnine, one may conclude that the patient passes into an ultra-cataleptic state from which he can only become normal by first becoming cataleptic again. The action of the carbon dioxide is probably to make the catalepsy more intense after the ultra-cataleptic phase has worn off.

Better results in catatonia are to be expected from a drug which decreases muscle tone, not one which increases it, like carbon dioxide. The object of such experiments in monkeys is to find a drug which will bring the cataleptic monkey back to normal, not one which causes it to pass into the ultra-cataleptic phase. It should be a drug which will keep the monkey normal for as long as possible.

11. Emphasis is laid on the fact that carbon dioxide, which is capable of causing and abolishing the cataleptic state, is a natural product of metabolism and that its concentration in the blood must depend

on the respiratory function. As it has frequently been observed clinically that schizophrenics appear to breathe very shallowly, a further investigation was carried out to establish this fact definitely and also to look for any other abnormality in the respiration of these patients.

Section II.

1. Although statements have previously been made by different observers that schizophrenics appear to breathe more shallowly than normal subjects, reports have been contradictory regarding the rate of respiration. The only experimental evidence has depended on instruments in the nature of rubber tubes fixed round the subject's chest. In no previous investigation has more than about a score of individuals been examined.

2. In the present study a plethysmographic apparatus was used by which the amount of air passing in and out of the chest (tidal air) could be measured. The rate was also recorded. With this instrument 62 normal subjects and 121 schizophrenics were examined. The schizophrenics were found to breathe more shallowly and more rapidly on the average than normals, the difference being significant. This did not apply to a group of 19 female melancholics nor 6 male melancholics.

3. It is pointed out that the type of respiration employed by the schizophrenics is an inefficient one. Allusion is made to the work of J.S.

Haldane and his pupils in which this rapid shallow type of respiration has been discussed. They have found that in most cases this was associated with oxygen desaturation of the arterial blood. This condition was found in cases of cyanosed schizophrenics by Hinsie and Segal.

4. Evidence is adduced that patients showing severe symptoms of catatonia breathe slowly as well as shallowly. Such cases however are less frequent in the modern mental hospitals where occupational therapy is employed. It is concluded that the increased rapidity of breathing among schizophrenics to some extent compensates for the diminished depth, but that when this fails, the severe catatonic state ensues with cyanosed extremities and torpor of mind. This state can be improved by enforced breathing exercises (G.F. Peters), and by occupational therapy generally.

5. It is remarked that the respiration in most catatonics does not resemble that found in the dozing or sleeping states. In mild catatonia the breathing is shallow but rapid, while in severe catatonia it becomes slower. In the drowsy state

which precedes sleep, the breathing is deep and very slow, while in sound sleep it becomes shallow and slightly more rapid.

6. Various observers, from the days of Kahlbaum and T.S. Clouston, have remarked on the frequency of tuberculosis among these patients in comparison with other types of mental disease. The results of the present study indicate that this is probably caused by the shallow type of respiration with insufficient expansion of the lungs, rather than the result of poor physique generally.

Section III.

1. The respiratory function is next studied in its relation to the higher cerebral centres. A description is given of previous work on the subject. Some earlier workers had studied the effects of various emotions, pleasant and unpleasant stimuli etc. on the respiratory rhythm. On the whole the results were disappointing.

2. F. Peterson and C.G. Jung indicated that changes of respiration were more closely related to conscious thought and vocalisation than to emotional changes. Golla and Antonovitch found that about fifty per cent of normal individuals breathed with regular rhythm and about fifty per cent with irregular rhythm. They stated that the regular breathers more commonly employed visual imagery as an instrument of thought, while the irregular employed predominantly auditory imagery, the tendency to vocalisation being responsible for the irregularity.

3. In the present enquiry, an attempt is made to answer three questions in relation to respiratory rhythm. (a) Is there any particular mental pro-

cess which in normal subjects gives rise to a special type of respiratory tracing? (b) Is there any feature which is more frequently found, or any feature which is only found, in the respiratory record of a psychotic individual as compared to a normal? (c) Are the respiratory reactions of psychotic subjects to various stimuli different from those of normal subjects?

4. The respiratory records of 65 normal subjects, and of 178 psychotics were examined. Of the normals, 32 breathed with a regular rhythm and 33 with an irregular rhythm. The various causes of irregularity of respiratory rhythm are investigated, and evidence is brought forward to show that auditory imagery with its tendency to vocalisation is responsible for this irregularity, when other causes have been excluded.

5. The following facts support this conclusion. Forty four normal individuals were set a problem, the solution of which would ordinarily demand visual imagery. Eighteen were regular in one task but irregular in the other. Of these 18, all except one showed regular rhythm in the test for

which visual imagery was indicated but irregular rhythm in the test for which auditory imagery was commonly used. Thirteen individuals were regular in both tests, and 13 irregular in both tests. Subjective examination of these individuals indicated that 12 of the 13 regular breathers employed predominantly visual imagery, while 10 of the 13 irregular breathers had a preference for auditory imagery.

6. Since visual and auditory images are more vivid in dreams, respiration was recorded while the subjects for experiment were in the hypnotic state. On waking from this state, a subject can readily recall whether he had been employing visual or auditory imagery. It was suggested to the subject that he was to do multiplication tables and that he would either hear someone recite them or see them on a board. It was considered that those who heard the tables were predominantly "auditory" thinkers, and those who saw them, predominantly "visual" thinkers. The following results were obtained. Of the 17 subjects -

8 saw the multiplication tables (Class 1)

5 heard a voice recite them (Class 2)

4 saw and heard simultaneously (Class 3)

The rhythm was examined of such subjects, (a) when awake, (b) when dreaming a visual dream, (c) when dreaming that they were listening to a tune.

Class (1) were all regular during the visual dream, and also when awake. Three of these were irregular during an auditory dream.

Class (2) were all irregular during the auditory dream. Four out of the five were irregular when awake, and two were irregular during the visual dream.

Class (3). Three of this class were irregular during the auditory dream, and three were regular during the visual dream. Three were regular when awake.

None of those who were regular throughout used auditory imagery from choice, and none of those who were irregular throughout used visual imagery from choice.

By these results the former conclusions are strengthened, namely that those who have a preference for visual imagery breathe regularly, while those with a preference for auditory imagery breathe irregularly.

These results were taken as showing that individuals vary considerably in their tendency to vocalise when thinking. Where this is present, the subject finds himself employing sound images, and his breathing is irregular. Where there is no tendency to vocalise, the respiration remains regular and the imagery is visual.

7. Of the 136 schizophrenics, 94 were regular and 42 irregular. When these were arranged in groups according to the length of time spent in hospital, of those who had been in hospital less than one year 38 per cent. were regular; of those from two to five years, 61 per cent. were regular; from 6 to 10 years, 80 per cent; 11 to 20 years, 82 per cent. and over 20 years 83 per cent. Thus among the groups who had been in hospital more than 5 years, the proportion of regular breathers was significantly higher. Of the 32 melancholic patients, only 3 of whom had been in hospital more than 5 years, 14 were regular and 18 irregular.

Of the epileptics who had been in hospital more than 20 years, 8 were regular and 1 irregular. These were all considerably demented. Of those who had been in less than 5 years, 2 were regular and 2 irregular.

8. There was no characteristic difference between the regular rhythm of normal subjects and that of schizophrenics. In the latter group, however, an extreme degree of regularity was more frequent. They also showed on the whole a shallower and more rapid rhythm. Some showed records of a peculiar character not found in normals. Those with hallucinations showed characteristic records, the extreme regularity being broken by extreme irregularity during the hallucinations, even when there was no movement of lips.

9. Reactions of the respiratory mechanism to stimuli were studied in normals and schizophrenics. Not enough cases were examined to give very definite results owing to the scatter among normal subjects. There was a significant difference, however, between the reaction of those schizophrenics who were able to perform an intellectual exercise,

and normals. The schizophrenics did not react with so great an increase of respiratory rate.

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TABLE I.

Showing the effect of different doses of carbon dioxide on monkeys made cataleptic by bulbocapnine. (see page 17)

Monkey's Number or Letter	Monkey's weight in grams	Dose of Bulbocapnine in mg.	Time in minutes after injection of bulbocapnine before CO_2	Dose of CO_2 per cent	Dose of CO_2 Minutes	Hanging time in seconds immediately before CO_2	Hanging time in seconds immediately after CO_2	Longest hang after CO_2 in seconds	Remarks
15 per cent CO_2									
10	2330	50	91	15	$1\frac{1}{2}$	22	20	19	CO_2 has no marked effect (See Chart 2).
6	4960	50	52	15	4	16	10	12	ditto.
8	2880	50	95	15	$1\frac{1}{2}$	55	12	48	Catalepsy maximal before CO_2 given (See Chart 6).
8	2880	50	109	15	6	17	26	26	Catalepsy almost disappeared when CO_2 given (See Chart 7).
25 per cent CO_2									
12	790	30	58	25	$1\frac{1}{2}$	38	46	46	Immediate increase of catalepsy.
6	4960	50	44	25	$1\frac{1}{2}$	11	17	17	ditto. (See Chart 3).
"J"	4030	75	70	25	$2\frac{1}{4}$	17	27	27	ditto.
"E"	3710	75	79	25	3	28	30	30	ditto but slight.
"C"	3730	75	73	25	3	14	20	20	Immediate increase of catalepsy.
35 per cent CO_2									
1	2790	75	42	35	1	35	2	22	CO_2 temporarily caused virtual abolition of catalepsy.
1	2790	75	106	35	1	21	3	19	ditto.
2	2580	75	58	35	4	19	4	16	ditto.
5	2810	50	26	35	4	37	0	34	CO_2 temporarily abolished catalepsy.
4	2950	75	46	35	4	29	0	19	ditto.
10	2330	50	98	35	4	41	0	22	ditto (See Chart 4).
50 per cent CO_2									
6	4960	50	54	50	1	14	0	23	ditto.

TABLE II.

Showing behaviour of the Hanging Response to various doses of Carbon Dioxide.
(see page 20)

Number of Monkey.	Weight in grams.	Percentage Concentration of Carbon Dioxide.	Length of Administration in minutes.	Whether Hanging Response present.	Whether Hanging Response is followed by period when monkey refuses to hang.	Time in seconds of longest hang.	Length of time in minutes That Hanging Response remained present.
5	2810	15	1½	Yes	No	2	Under 1
		15	3	No	-		
		15	4½	No	-		
		15	6	No	-		
		25	1½	Yes	No	21	Under 1
		40	1½	Yes	Doubtful	31	Under 1
		40	2½	Yes	Yes	30	27
		40	5	Yes	Yes		7
6	4960	15	1½	No			
		15	4½	Yes	Doubtful	3	Under 1
		15	6	No			
		15	6	Yes	No	18	Under 1
		25	1½	Yes	No	35	1
		25	2½	Yes	No	21	2
		40	1½	Yes	Yes	25	2
		40	2½	Yes	Yes	25	15
8	2880	15	1½	Yes	No	11	Under 1
		15	6	Yes	No	53	7
		25	1½	Yes	No	19	2
		25	2½	Yes	No	17	2
		40	1½	Yes	Yes	50	1
		40	2½	Yes	Yes	33	9
9	2890	15	1½	No			
		15	4½	No			
		15	6	No			Under 1
		25	2½	Yes	No	2	Under 1
		40	1½	Yes	Doubtful	30	Under 1
		40	2½	Yes	Yes	16	2
		40	5	Yes	Yes		3½
10	2330	15	1½	Yes	No	14	1½
		15	3	Yes	No	48	20
		15	4½	Yes	No	64	6
		15	6	Yes	No	33	10
		25	1½	Yes	No	45	4
		25	2½	Yes	No	65	6½
		40	1½	Yes	Doubtful	49	Under 1
		40	2½	Yes	Yes	47	45
		40	5	Yes	Yes	48	9